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LOGINID:ssspta1611sxp

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
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NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
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NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
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NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
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NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA

NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42 Jun 06 Simultaneous left and right truncation added to CBNB
NEWS 43 Jun 06 PASCAL enhanced with additional data
NEWS 44 Jun 20 2003 edition of the FSTA Thesaurus is now available
NEWS 45 Jun 25 HSDB has been reloaded

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:06:37 ON 01 JUL 2003

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:06:42 ON 01 JUL 2003
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STRUCTURE FILE UPDATES: 30 JUN 2003 HIGHEST RN 540462-79-1
DICTIONARY FILE UPDATES: 30 JUN 2003 HIGHEST RN 540462-79-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s 220488-46-OP/RN

```
L1            0 220488-46-OP/RN

=> d l1
L1 HAS NO ANSWERS
L1             0 SEA FILE=REGISTRY PLU=ON  220488-46-OP/RN


=> s l1
L2            0 220488-46-OP/RN

=> d 220488-46-OP/RN
'220488-46-OP' MUST END IN '/Q', '/A', '/L', '/S' OR '/B'
The saved name for a query (or structure or screen set) must end with
'/Q'.  The saved name for an answer set must end with '/A'.  The saved
name for an L# list must end with '/L'.  SDI request names must end
with '/S'.  To see a list of all saved query, answer set,, and L# list
names for this loginid, enter "DISPLAY SAVED" at an arrow
prompt (=>).  Enter "DISPLAY SAVED/S" to see a list of SDI request
names.  Enter "DISPLAY SAVED/B" to see a list of BATCH search
requests.

=> d 220488-46-OP/RN/Q
'220488-46-OP' MUST END IN '/Q', '/A', '/L', '/S' OR '/B'
The saved name for a query (or structure or screen set) must end with
'/Q'.  The saved name for an answer set must end with '/A'.  The saved
name for an L# list must end with '/L'.  SDI request names must end
with '/S'.  To see a list of all saved query, answer set,, and L# list
names for this loginid, enter "DISPLAY SAVED" at an arrow
prompt (=>).  Enter "DISPLAY SAVED/S" to see a list of SDI request
names.  Enter "DISPLAY SAVED/B" to see a list of BATCH search
requests.

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               2.40       2.61

FILE 'CAPLUS' ENTERED AT 14:10:21 ON 01 JUL 2003
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COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
```



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FILE COVERS 1907 - 1 Jul 2003  VOL 139 ISS 1
FILE LAST UPDATED: 30 Jun 2003  (20030630/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
```

```
=> s 130:168387?DN
'?' TRUNCATION SYMBOL NOT VALID WITHIN '168387?DN'
The truncation symbol ?  may be used only at the end of a search
term.  To specify a variable character within a word use '!', e.g.,
'wom!n' to search for both 'woman' and 'women'.  Enter "HELP
TRUNCATION" at an arrow prompt (=>) for more information.

=> s 130:168387/DN
L3            1 130:168387/DN

=> d l3 fbib hitstr abs total

L3   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
AN   1999:113656  CAPLUS
DN   130:168387
TI   Irreversible inhibitors of tyrosine kinases
IN   Bridges, Alexander James
PA   Warner-Lambert Company, USA
SO   PCT Int. Appl., 124 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 9906378         A1   19990211       WO 1998-US15784  19980729
         W:  AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS,
             JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG,
             SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                            US 1997-54060P P 19970729
     AU 9887607          A1   19990222       AU 1998-87607    19980729
                                            US 1997-54060P P 19970729
                                            WO 1998-US15784W 19980729
     US 6127374          A    20001003       US 1999-269545   19990325
                                            US 1997-54060P P 19970729
                                            WO 1998-US15784W 19980729
     US 6562818          B1   20030513       US 2000-593031   20000613
                                            US 1997-54060P P 19970729
                                            WO 1998-US15784W 19980729
                                            US 1999-269545 A319990325
OS   MARPAT 130:168387
AB   Pyrimidine derivs. that are irreversible inhibitors of tyrosine kinases
     are reported.  Thus, PhCH2OH was treated with 4-FC6H4NO2 to give
     4-PhCH2OC6H4NO2, which was reduced to the amine and used to aminate
     4-chloro-6-nitroquinazoline hydrochloride.  The resulting
     6-nitro-4-(4-benzyloxyanilino)quinazoline hydrochloride was reduced to the
     amine and acylated to give N-[4-(4-benzyloxyanilino)quinazolin-6-
     yl]acrylamide (I).  I had an IC50 for inhibition of epidermal growth
     factor receptor tyrosine kinase of 3.6 nM.
RE.CNT  9     THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
=> log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               6.22       8.83

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                              -0.65      -0.65

STN INTERNATIONAL LOGOFF AT 14:13:38 ON 01 JUL 2003
```

L4 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 1994:217715 CAPLUS
DN 120:217715
TI Quinazoline tyrosine kinase-inhibiting anticancer agents
IN Barker, Andrew J.
PA Zeneca Ltd., UK
SO Can. Pat. Appl., 99 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2086968	AA	19930721	CA 1993-2086968	19930108
	CA 2086968	C	19980623		
				GB 1992-1095	A 19920120
				GB 1992-13572	A 19920626
				GB 1992-23735	A 19921112
	ZA 9300015	A	19930720	ZA 1993-15	19930104
				GB 1992-1095	A 19920120
	AU 9331010	A1	19930722	AU 1993-31010	19930104
	AU 661533	B2	19950727		
				GB 1992-1095	A 19920120
				GB 1992-13572	A 19920626
				GB 1992-23735	A 19921112
	HU 63153	A2	19930728	HU 1993-94	19930115
				GB 1992-1095	A 19920120
				GB 1992-13572	A 19920626

<7/1/2003>

Patel

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NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
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NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
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NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
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NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
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NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA

```
 NEWS 41  May 19  RAPRA enhanced with new search field, simultaneous left and
                  right truncation
 NEWS 42  Jun 06  Simultaneous left and right truncation added to CBNB
 NEWS 43  Jun 06  PASCAL enhanced with additional data
 NEWS 44  Jun 20  2003 edition of the FSTA Thesaurus is now available
 NEWS 45  Jun 25  HSDB has been reloaded

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:38:38 ON 01 JUL 2003

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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STRUCTURE FILE UPDATES:   30 JUN 2003  HIGHEST RN 540462-79-1
DICTIONARY FILE UPDATES:  30 JUN 2003  HIGHEST RN 540462-79-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
```

```
Uploading 10016280.5

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
```

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1
SAMPLE SEARCH INITIATED 14:39:14 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    302 TO ITERATE

100.0% PROCESSED     302 ITERATIONS                          7 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         4998 TO     7082
PROJECTED ANSWERS:               7 TO      298

L2            7 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 14:39:21 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   6071 TO ITERATE

100.0% PROCESSED    6071 ITERATIONS                         82 ANSWERS
SEARCH TIME: 00.00.01

L3           82 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             148.15     148.36

FILE 'CAPLUS' ENTERED AT 14:39:27 ON 01 JUL 2003
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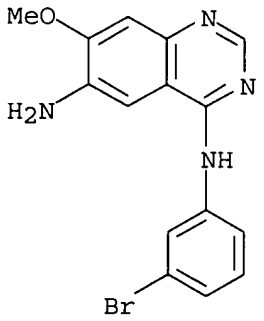
FILE COVERS 1907 - 1 Jul 2003  VOL 139 ISS 1
FILE LAST UPDATED: 30 Jun 2003  (20030630/ED)
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 24 L3

=> d l4 fbib hitstr abs total

L4 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2002:951575 CAPLUS
DN 138:117246
TI Mapping the Binding Site of a Large Set of Quinazoline Type EGF-R Inhibitors Using Molecular Field Analyses and Molecular Docking Studies
AU Hou, Tingjun; Zhu, Lili; Chen, Lirong; Xu, Xiaojie
CS College of Chemistry and Molecular Engineering, Peking University, Beijing, 100871, Peop. Rep. China
SO Journal of Chemical Information and Computer Sciences (2003), 43(1), 273-287
CODEN: JCISD8; ISSN: 0095-2338
PB American Chemical Society
DT Journal
LA English
IT **171745-06-5**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(QSAR (quant. structure-activity relationship) studies on quinazoline type epidermal growth factor receptors (EGF-R) inhibitors using mol. field analyses and mol. docking studies)
RN 171745-06-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



AB In the current work, three-dimensional QSAR studies for one large set of quinazoline type epidermal growth factor receptor (EGF-R) inhibitors were conducted using two types of mol. field anal. techniques:comparative mol. field anal. (CoMFA) and comparative mol. similarity indexes anal. (CoMSIA). These compds. belonging to six different structural classes were randomly divided into a training set of 122 compds. and a test set of 13 compds. The statistical results showed that the 3D-QSAR models derived from CoMFA were superior to those generated from CoMSIA. The most optimal CoMFA model after region focusing bears significant cross-validated r2cv of 0.60 and conventional r2 of 0.92. The predictive power of the best

CoMFA model was further validated by the accurate estn. to these compds. in the external test set, and the mean agreement of exptl. and predicted log(IC50) values of the inhibitors is 0.6 log unit. Sep. CoMFA models were conducted to evaluate the influence of different partial charges (Gasteiger-Marsili, Gasteiger-Huckel, MMFF94, ESP-AM1, and MPA-AM1) on the statistical quality of the models. The resulting CoMFA field map provides information on the geometry of the binding site cavity and the relative wts. of various properties in different site pockets for each of the substrates considered. Moreover, in the current work, we applied MD simulations combined with MM/PBSA (Mol. mechanics/Possion-Boltzmann Surface Area) to det. the correct binding mode of the best inhibitor for which no ligand-protein crystal structure was present. To proceed, we define the following procedure: three hundred picosecond mol. dynamics simulations were first performed for the four binding modes suggested by DOCK 4.0 and manual docking, and then MM/PBSA was carried out for the collected snapshots. The most favorable binding mode identified by MM/PBSA has a binding free energy about 10 kcal/mol more favorable than the second best one. The most favorable binding mode identified by MM/PBSA can give satisfactory explanation of the SAR data of the studied mols. and is in good agreement with the contour maps of CoMFA. The most favorable binding mode suggests that with the quinazoline-based inhibitor, the N3 atom is hydrogen-bonded to a water mol. which, in turn, interacts with Thr 766, not Thr 830 as proposed by Wissner et al. (J. Med. Chem. 2000, 43, 3244). The predicted complex structure of quinazoline type inhibitor with EGF-R as well as the pharmacophore mapping from CoMFA can interpret the structure activities of the inhibitors well and afford us important information for structure-based drug design.

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2002:487536 CAPLUS
DN 137:63250
TI Quinazoline derivatives as inhibitors of human EFG tyrosine kinase
IN Himmelsbach, Frank; Langkopf, Elke; Blech, Stefan; Jung, Birgit; Baum, Elke; Solca, Flavio
PA Boehringer Ingelheim Pharma Kg, Germany
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002050043	A1	20020627	WO 2001-EP14569	20011212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			DE 2000-10063435A	20001220
DE 10063435	A1	20020704	DE 2000-10063435	20001220
AU 2002019174	A5	20020701	AU 2002-19174	20011212
			DE 2000-10063435A	20001220

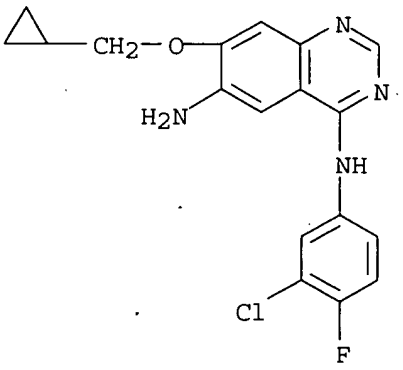
US 2002173509 A1 20021121 WO 2001-EP14569W 20011212
US 2001-23099 20011217
DE 2000-10063435A 20001220
US 2000-259201PP 20001228

OS MARPAT 137:63250

IT **290304-07-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

RN 290304-07-3 CAPLUS

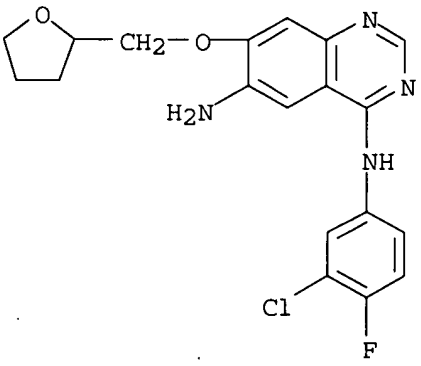
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



IT **314771-75-0P 314771-76-1P 314771-77-2P**
402855-03-2P 402855-04-3P 402855-05-4P
439081-58-0P 439081-59-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

RN 314771-75-0 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2-furanyl)methoxy]- (9CI) (CA INDEX NAME)

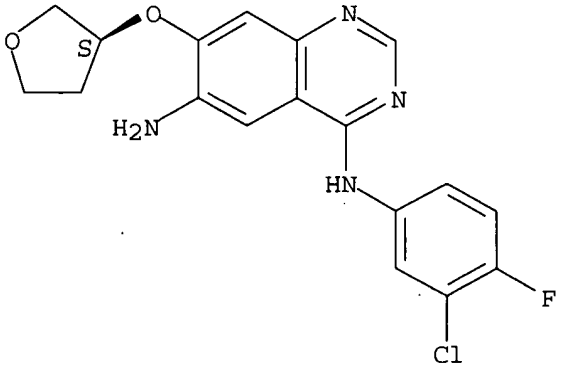


RN 314771-76-1 CAPLUS

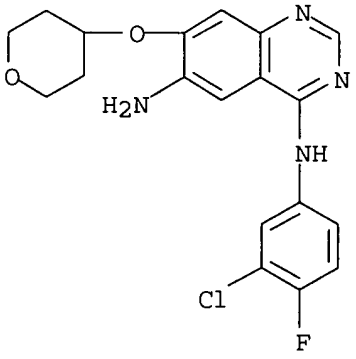
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(3S)-tetrahydro-3-

furanyl]oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

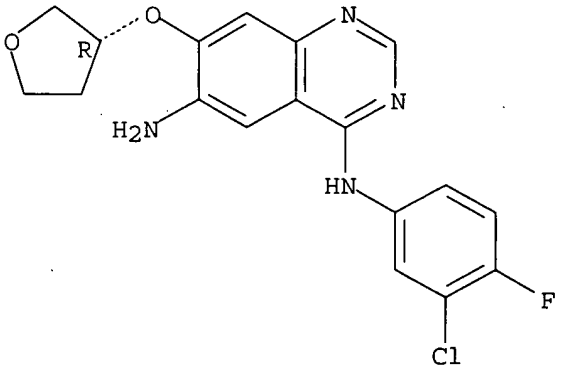


RN 314771-77-2 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2H-pyran-4-yl)oxy]- (9CI) (CA INDEX NAME)

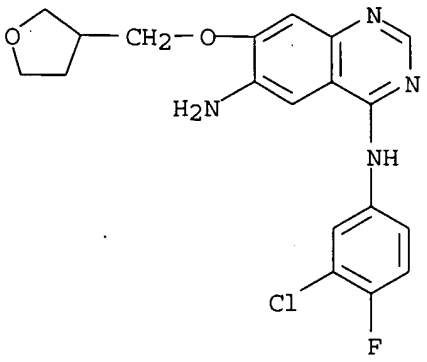


RN 402855-03-2 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(3R)-tetrahydro-3-furanyl]oxy]- (9CI) (CA INDEX NAME)

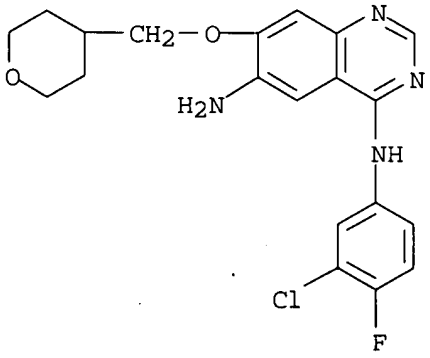
Absolute stereochemistry.



RN 402855-04-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-3-furanyl)methoxy]- (9CI) (CA INDEX NAME)

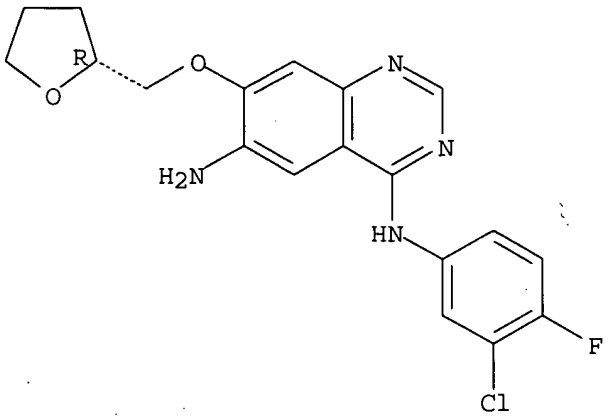


RN 402855-05-4 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2H-pyran-4-yl)methoxy]- (9CI) (CA INDEX NAME)



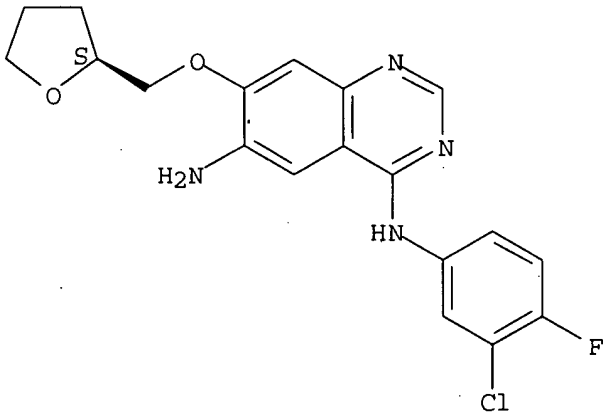
RN 439081-58-0 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(2R)-tetrahydro-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 439081-59-1 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(2S)-tetrahydro-2-furanyl]methoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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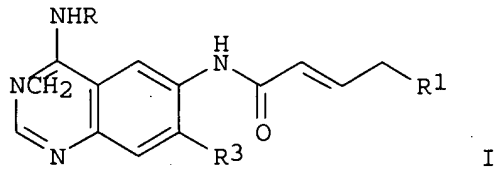

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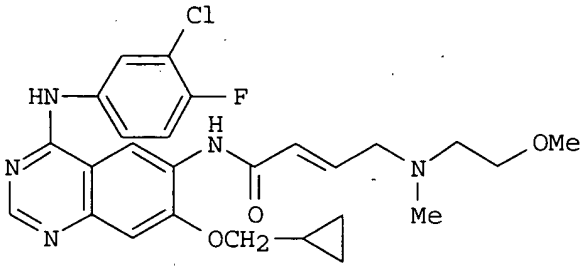


II

AB Quinazoline derivs. I [R = PhCH2, PhCHMe, 3,4-Cl(F)C6H3; R1 = NMeR2, NEt2, NEtCH2CH2OMe, N(CH2CH2OMe)2, morpholino; R2 = Me, Et, CHMe2, cyclopropyl, CH2CH2OMe, 3-tetrahydrofuryl, 2-tetrahydrofurylmethyl, 3-tetrahydrofurylmethyl, 4-tetrahydropyranyl, 4-tetrahydropyranylmethyl; R3 = cyclopropylmethoxy, cyclobutyloxy, cyclopentyloxy, 3-tetrahydrofuranyloxy, 2-tetrahydrofuranylmethoxy, 3-tetrahydrofuranylmethoxy, 4-tetrahydropyranyloxy, 4-tetrahydropyranylmethoxy] were prepd. for use as inhibitors of signal transduction caused by human EFG receptor tyrosine kinase. They are useful in the treatment of tumoral diseases, diseases of the lung and the respiratory tract, the gastrointestinal tract, and the gallbladder and bile ducts. Thus, the quinazoline II was prepd. by converting bromocrotonic acid to its chloride, and reaction with 4-[(3-chloro-4-fluorophenyl)amino]-6-amino-7-cyclopropylmethoxyquinazoline, followed by MeNHCH2CH2OMe. II had an IC50 against human EFG receptor kinase of 0.7 nM.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2002:171892 CAPLUS
DN 136:216762
TI Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PA Boehringer Ingelheim Pharma Kg, Germany
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002018376	A1	20020307	WO 2001-EP9536	20010818

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 2000-10042062A 20000826

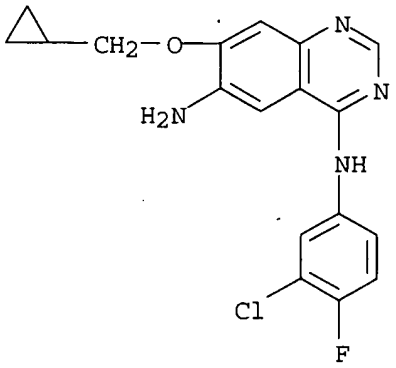
DE 10042062	A1	20020307	DE 2000-10042062 20000826
AU 2001095482	A5	20020313	AU 2001-95482 20010818
			DE 2000-10042062A 20000826
			WO 2001-EP9536 W 20010818
EP 1315720	A1	20030604	EP 2001-976108 20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
			DE 2000-10042062A 20000826
			WO 2001-EP9536 W 20010818
US 2002115675	A1	20020822	US 2001-934631 20010822
			DE 2000-10042062A 20000826
			US 2000-230542PP 20000905

OS MARPAT 136:216762

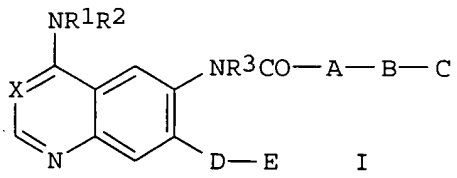
IT **290304-07-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (amino)(heterocyclylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 290304-07-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



GI



I

AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 =

(substituted) Ph, PhCH2, 1-phenylethyl; R3 = H, Me; A = (substituted) vinyl, ethynyl, 1,3-butadien-1,4-yl; B = (substituted) alkenyl, alkenylcarbonyl, etc.; C = (substituted) 2-oxomorpholin-4-yl, etc; D = oxyalkenyl, O; E = (substituted) amino, alkenylimino, imidazolyl, cycloalkyl; or DE = H, (substituted) alkoxy, etc.], were prepd. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(ethoxycarbonylmethyl)-N-((R)-2-hydroxy-3-methoxypropyl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline (prepn. given) and MeSO2OH in MeCN were stirred for 4 h under reflux to give 69% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[(R)-2-methoxymethyl-6-oxomorpholin-4-yl]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 2 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2002:171891 CAPLUS
DN 136:216761
TI Preparation of 4-amino-6-vinylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PA Boehringer Ingelheim Pharma Kg, Germany
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

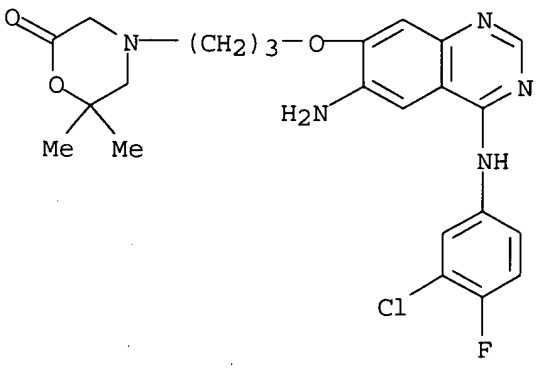
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002018375	A1	20020307	WO 2001-EP9534	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			DE 2000-10042064A	20000826
DE 10042064	A1	20020307	DE 2000-10042064	20000826
AU 2002010444	A5	20020313	AU 2002-10444	20010818
			DE 2000-10042064A	20000826
			WO 2001-EP9534 W	20010818
US 6403580	B1	20020611	US 2001-935498	20010823
			DE 2000-10042064A	20000826
			US 2000-230541PP	20000905

OS MARPAT 136:216761
IT **402723-54-0P 402723-56-2P 402723-58-4P**
402723-60-8P 402723-61-9P 402723-62-0P
402723-63-1P 402723-64-2P 402723-94-8P
402723-95-9P 402723-96-0P 402723-97-1P
402723-98-2P 402723-99-3P 402724-00-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

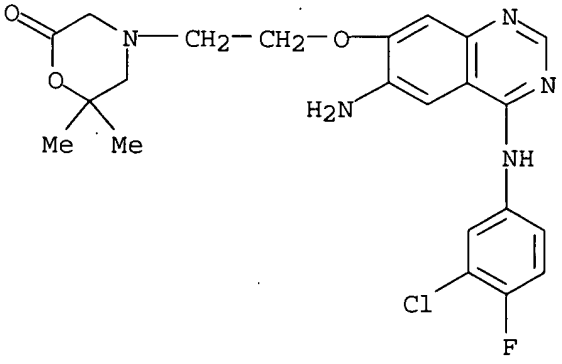
RN 402723-54-0 CAPLUS

CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



RN 402723-56-2 CAPLUS

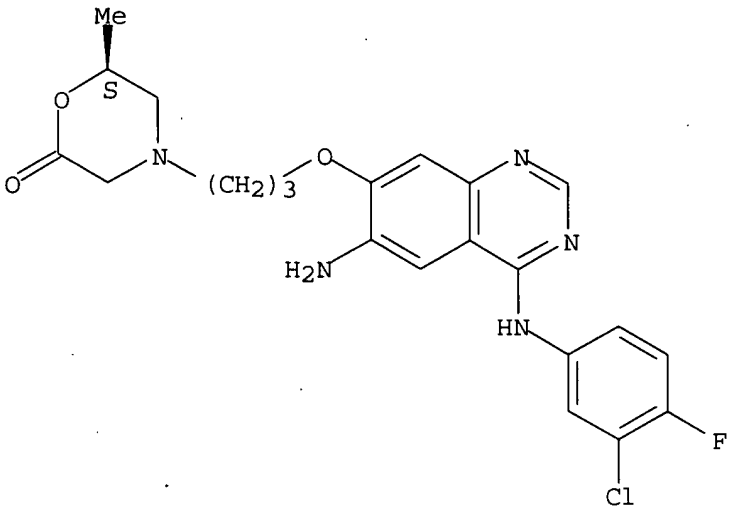
CN 2-Morpholinone, 4-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



RN 402723-58-4 CAPLUS

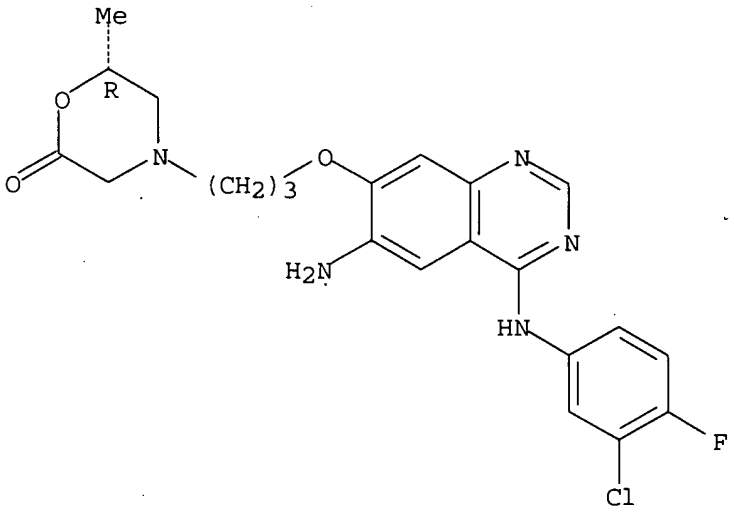
CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



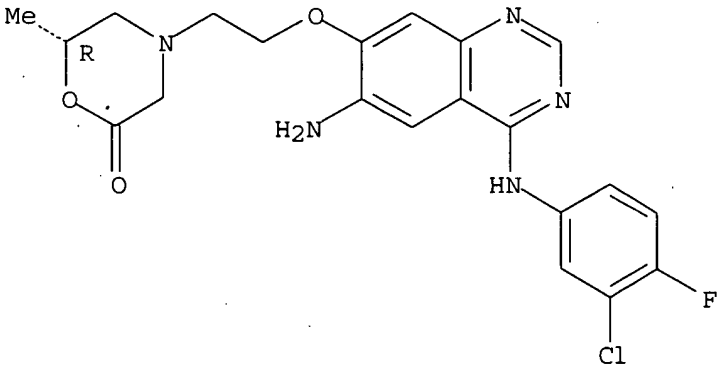
RN 402723-60-8 CAPLUS
CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



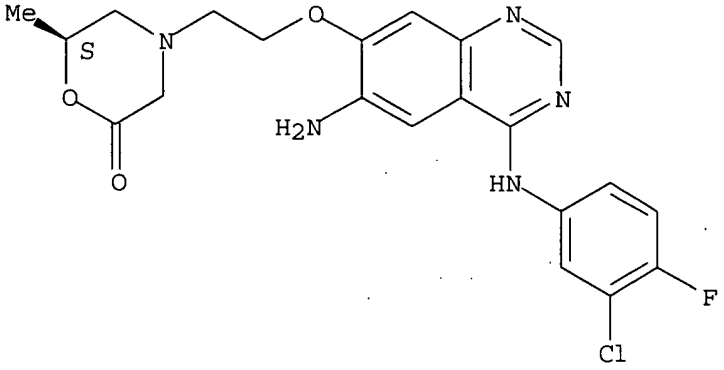
RN 402723-61-9 CAPLUS
CN 2-Morpholinone, 4-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



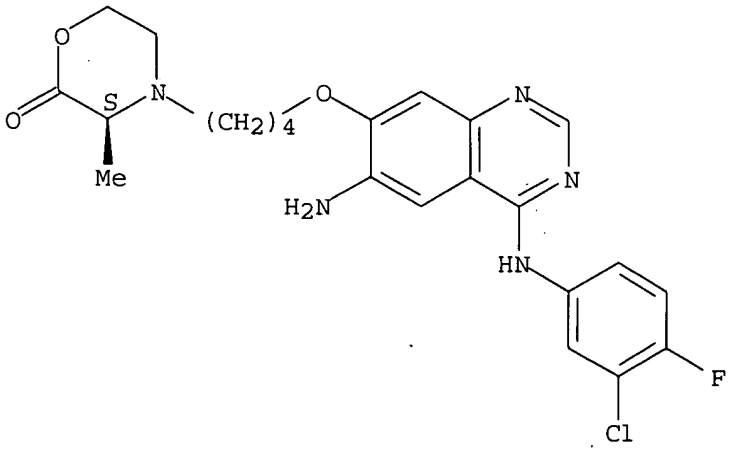
RN 402723-62-0 CAPLUS
CN 2-Morpholinone, 4-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

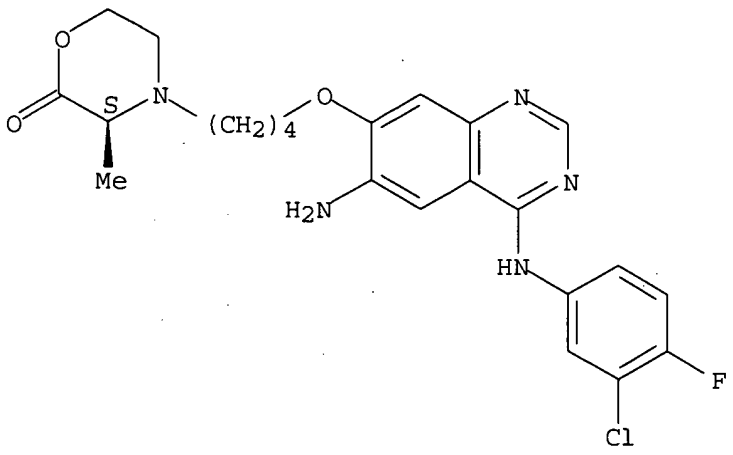
Absolute stereochemistry.



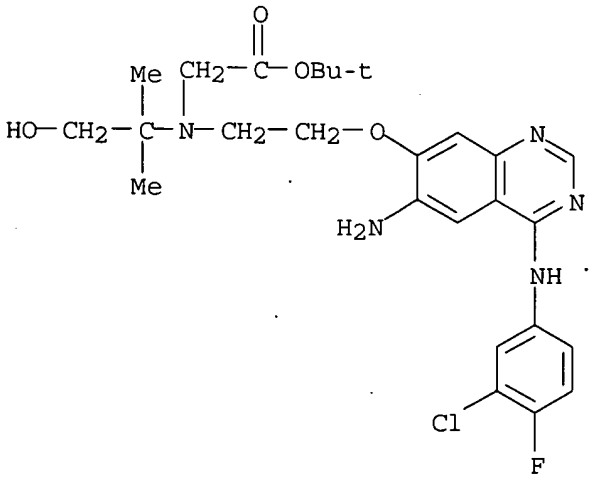
RN 402723-63-1 CAPLUS
CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-3-methyl-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

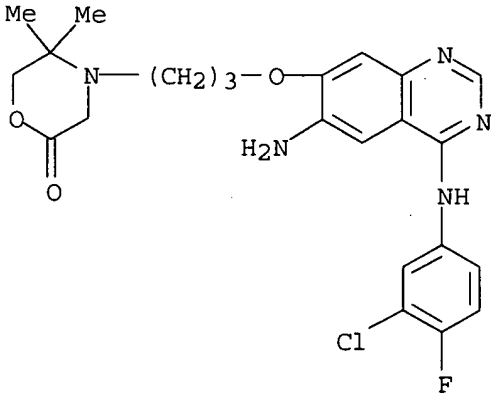




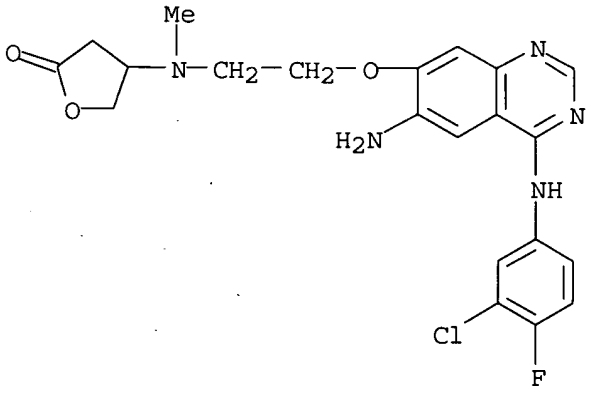
RN 402723-64-2 CAPLUS
CN Glycine, N-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-N-(2-hydroxy-1,1-dimethylethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



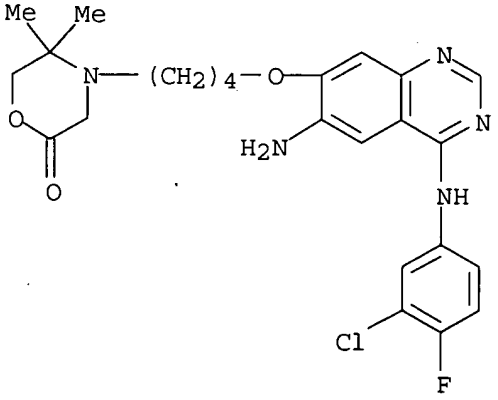
RN 402723-94-8 CAPLUS
CN 2-Morpholinone, 4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-5,5-dimethyl- (9CI) (CA INDEX NAME)



RN 402723-95-9 CAPLUS
CN 2(3H)-Furanone, 4-[[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]methylamino]dihydro- (9CI) (CA INDEX NAME)

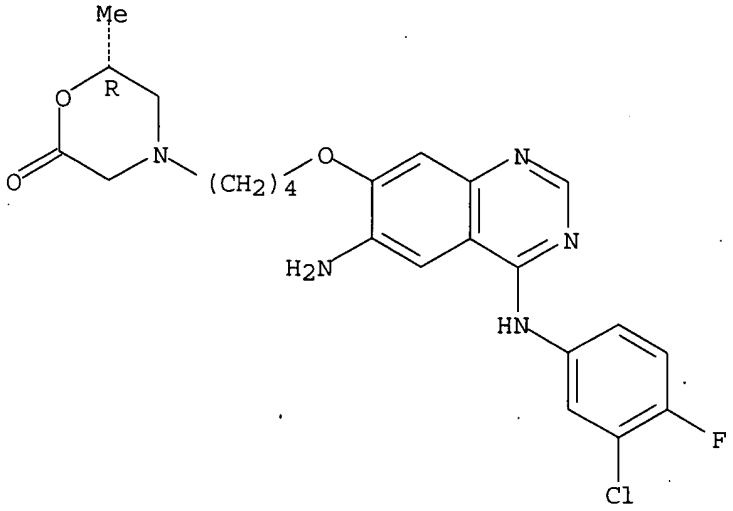


RN 402723-96-0 CAPLUS
CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-5,5-dimethyl- (9CI) (CA INDEX NAME)



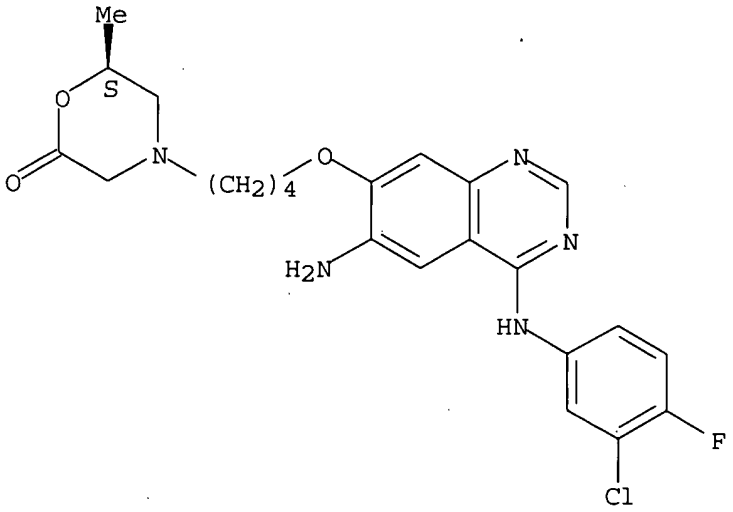
RN 402723-97-1 CAPLUS
CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-6-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

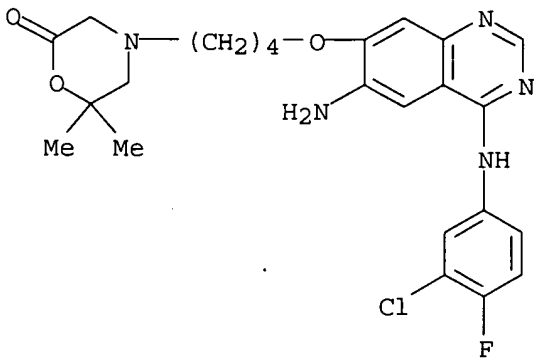


RN 402723-98-2 CAPLUS
CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-6-methyl-, (6S)- (9CI) (CA INDEX NAME)

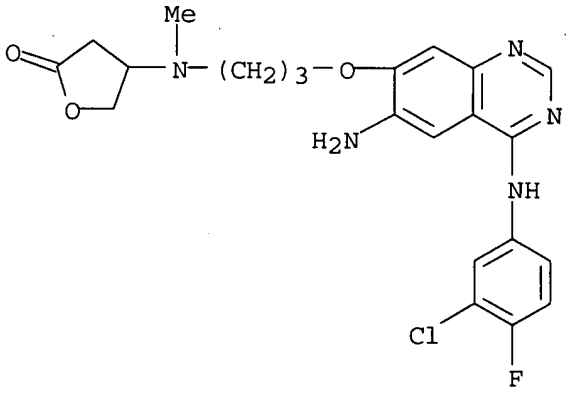
Absolute stereochemistry.



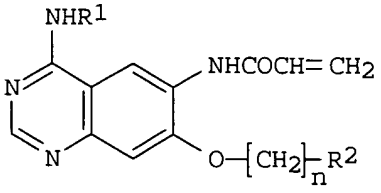
RN 402723-99-3 CAPLUS
CN 2-Morpholinone, 4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-6,6-dimethyl- (9CI) (CA INDEX NAME)



RN 402724-00-9 CAPLUS
CN 2(3H)-Furanone, 4-[[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]methylamino]dihydro- (9CI) (CA INDEX NAME)



GI



AB Title compds. [I; R1 = PhCH2, 1-phenylethyl, (substituted) Ph; R2 = N-(2-oxotetrahydrofuran-4-yl)methylamino, N(CH2CO2R3)2, (substituted) R4OCOCH2NCH2CH2OH, 2-oxomorpholin-4-yl; R3 = H, Me, Et; R4 = H, alkyl; n = 2-4],were prepd. Thus, a mixt. of CH2:CHCO2H and Et3N was stirred for 1 h at -50.degree. with CH2:CHCO2Cl in THF followed by addn. of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-oxomorpholin-4-yl)propyloxy]quinazoline (prepn. given) in THF at -55.degree. and slowly heating up at 0.degree. up to completely conversion to give 60% 4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(2,2-dimethyl-6-

oxomorpholin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. One of the exemplified examples, 4-[(R)-(1-phenylethyl)amino]-7-[2-(2,2-dimethyl-6-oxomorpholin-4-yl)ethoxy]-6-[(vinylcarbonyl)amino]quinazoline, inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.4 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

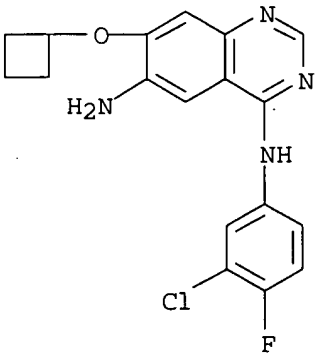
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2002:171889 CAPLUS
DN 136:232315
TI Preparation of 4-amino-6-vinylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PA Boehringer Ingelheim Pharma Kg, Germany
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

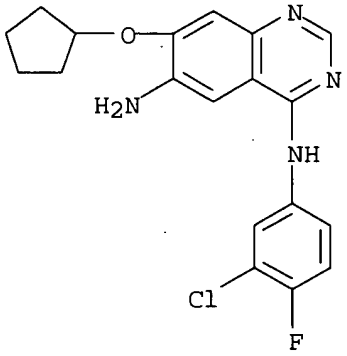
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002018373	A1	20020307	WO 2001-EP9537	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			DE 2000-10042060A	20000826
DE 10042060	A1	20020307	DE 2000-10042060	20000826
US 2002077330	A1	20020620	US 2001-929931	20010815
			DE 2000-10042060A	20000826
			US 2000-230389PP	20000906
AU 2001084021	A5	20020313	AU 2001-84021	20010818
			DE 2000-10042060A	20000826
			WO 2001-EP9537 W	20010818
EP 1315717	A1	20030604	EP 2001-962953	20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
			DE 2000-10042060A	20000826
			WO 2001-EP9537 W	20010818

OS MARPAT 136:232315
IT **290303-28-5P 290303-32-1P 290304-07-3P**
314771-75-0P 314771-76-1P 314771-77-2P
402855-01-0P 402855-03-2P 402855-04-3P
402855-05-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)
RN 290303-28-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclobutyloxy)-

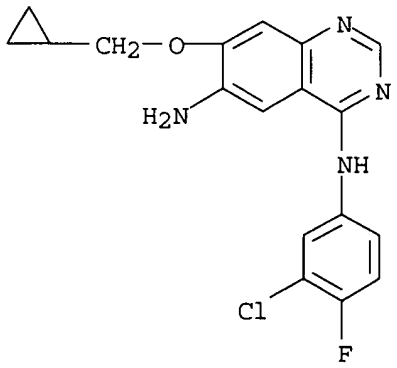
(9CI) (CA INDEX NAME)



RN 290303-32-1 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopentyloxy)-
(9CI) (CA INDEX NAME)

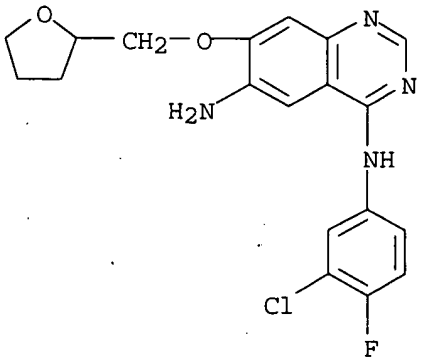


RN 290304-07-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-
(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



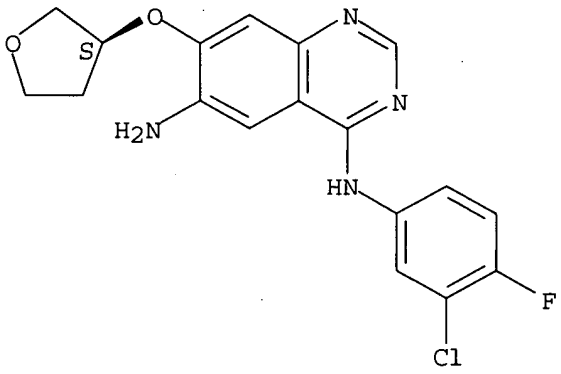
RN 314771-75-0 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2-

furanyl)methoxy]- (9CI) (CA INDEX NAME)

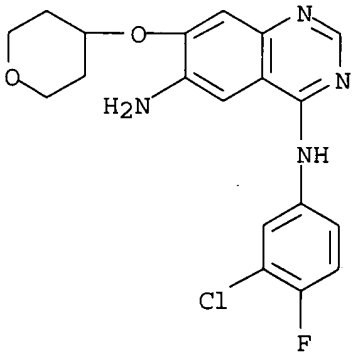


RN 314771-76-1 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(3S)-tetrahydro-3-furanyl]oxy]- (9CI) (CA INDEX NAME)

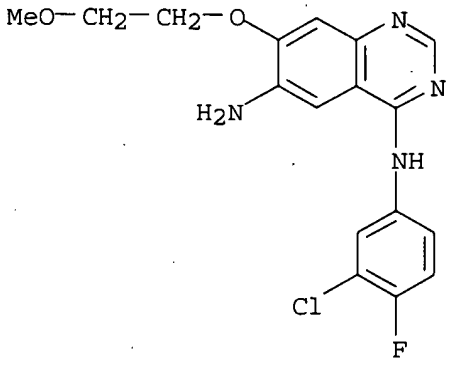
Absolute stereochemistry.



RN 314771-77-2 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2H-pyran-4-yl)oxy]- (9CI) (CA INDEX NAME)

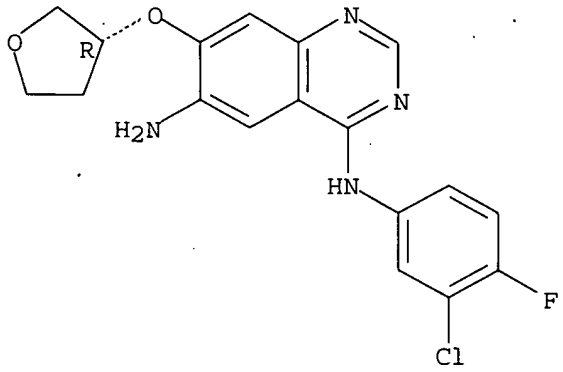


RN 402855-01-0 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(2-methoxyethoxy)-(9CI) (CA INDEX NAME)

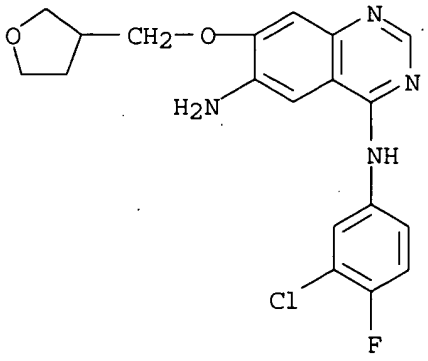


RN 402855-03-2 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(3R)-tetrahydro-3-furanyl]oxy]- (9CI) (CA INDEX NAME)

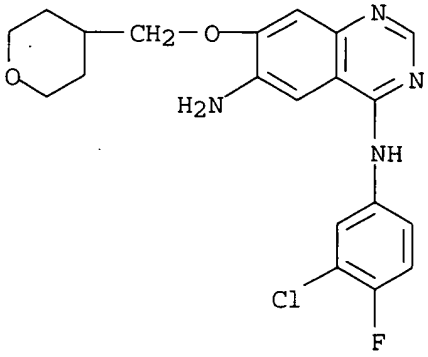
Absolute stereochemistry.



RN 402855-04-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-3-furanyl)methoxy]- (9CI) (CA INDEX NAME)



RN 402855-05-4 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[(tetrahydro-2H-pyran-4-yl)methoxy]- (9CI) (CA INDEX NAME)



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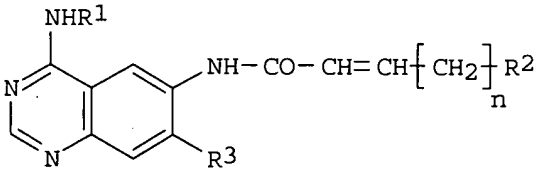


I

AB Title compds. [I; R1 = PhCH2, 1-phenylethyl, (substituted) Ph; R2 = N-[(1,3-dioxolan-2-yl)methyl]methylamino, (substituted) R4OCOCH2NCH2CH2OH, 2-oxomorpholin-4-yl; R4 = H, alkyl; R3 = H, (alkoxy)alkoxy, cycloalkylalkoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy; n = 1-3], were prepd. Thus, a mixt. of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-cyclopropylmethoxyquinazoline (prepn. given) and disopropylethylamine in THF was dropwise treated under ice-cooling with BrCH2CH:CHCO2Cl (prepn. given) in CH2Cl2 followed by stirring for 1 h under ice-cooling and for 2 h at room temp. and addn. of (S)-(2-hydroxypropylamino)acetic acid tert-Bu ester in CH2Cl2 to give after stirring over night at room temp. and stirring for 5 h at 60.degree.

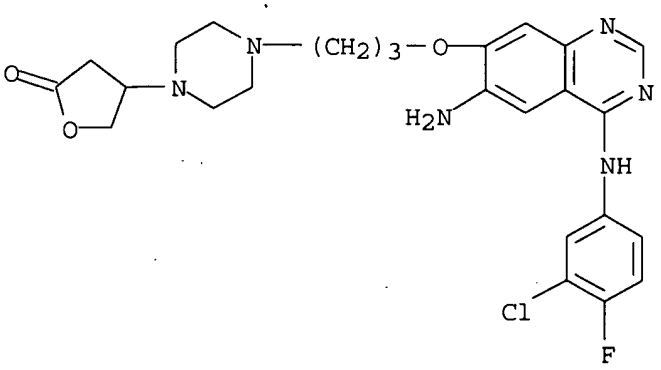
64% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(tert-butyloxycarbonylmethyl)-N-((S)-2-hydroxyprop-1-yl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. Several I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.02-15 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2002:171886 CAPLUS
DN 136:216758
TI Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PA Boehringer Ingelheim Pharma Kg, Germany
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

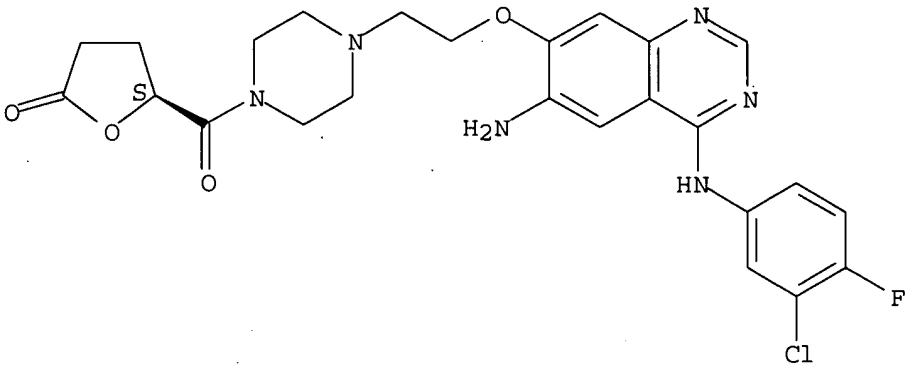
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002018370	A1	20020307	WO 2001-EP9535	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			DE 2000-10042061A	20000826
DE 10042061	A1	20020307	DE 2000-10042061	20000826
AU 2001089814	A5	20020313	AU 2001-89814	20010818
			DE 2000-10042061A	20000826
			WO 2001-EP9535 W	20010818
EP 1315716	A1	20030604	EP 2001-969610	20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
			DE 2000-10042061A	20000826
			WO 2001-EP9535 W	20010818
US 2002082270	A1	20020627	US 2001-934753	20010822
			DE 2000-10042061A	20000826
			US 2000-230119PP	20000905

OS MARPAT 136:216758
IT **402496-48-4P 402496-50-8P 402496-52-0P**
402496-81-5P 402496-83-7P 402497-08-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (amino)(heterocyclylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)
RN 402496-48-4 CAPLUS
CN 2(3H)-Furanone, 4-[4-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-1-piperazinyl]dihydro- (9CI) (CA INDEX NAME)

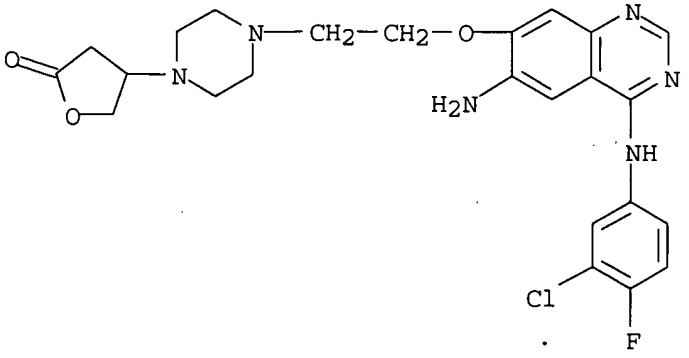


RN 402496-50-8 CAPLUS
CN Piperazine, 1-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-4-[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

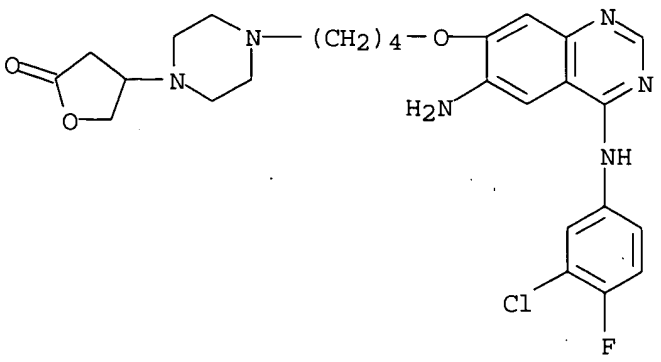


RN 402496-52-0 CAPLUS
CN 2(3H)-Furanone, 4-[4-[2-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]ethyl]-1-piperazinyl]dihydro- (9CI) (CA INDEX NAME)



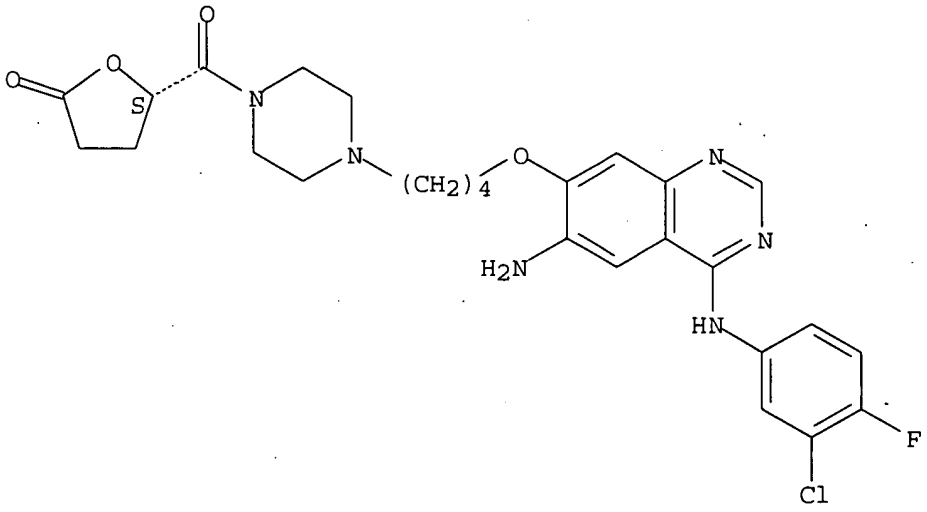
RN 402496-81-5 CAPLUS
CN 2(3H)-Furanone, 4-[4-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-

quinazolinyl]oxy]butyl]-1-piperazinyl]dihydro- (9CI) (CA INDEX NAME)



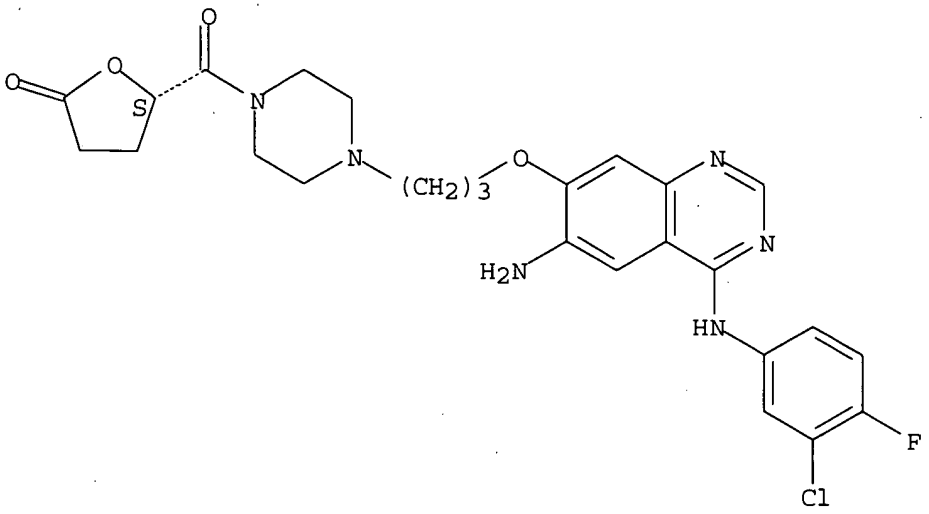
RN 402496-83-7 CAPLUS
CN Piperazine, 1-[4-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]butyl]-4-[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 402497-08-9 CAPLUS
CN Piperazine, 1-[3-[[6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-quinazolinyl]oxy]propyl]-4-[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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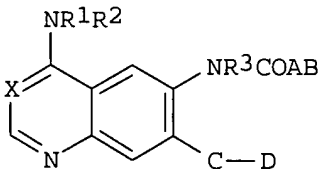


AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 = (substituted) Ph, PhCH2, 1-phenylethyl; R3 = H, Me; A = (substituted) vinyl, ethynyl, 1,3-butadien-1,4-yl; B = H, (substituted) alkyl, alkylcarbonyl, CO2H, alkoxycarbonyl, aminocarbonyl, (di)alkylaminocarbonyl, pyrrolidinylcarbonyl, piperidinylcarbonyl, morpholinocarbonyl, alkylpiperazinylcarbonyl; C = (oxy)alkenyl, O; D = (substituted) pyrrolidinyl, piperidinyl, hexahydroazepinyl, piperazinyl, etc.], were prepd. Thus, a mixt. of CH2:CHCO2H and Et3N was stirred for 45 min at -50.degree. with CH2:CHCO2Cl in THF followed by dropwise addn. of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-(3-[4-(2-oxotetrahydrofuran-4-yl)piperazin-1-yl]propyloxy)quinazoline (prepn. given) in THF for 20 min and stirring at 0.degree. up to completely conversion to give 31% 4-[(3-chloro-4-fluorophenyl)amino]-7-(3-[4-(2-oxotetrahydrofuran-4-yl)piperazin-1-yl]propyloxy)-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 12 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2001:762992 CAPLUS
DN 135:303907

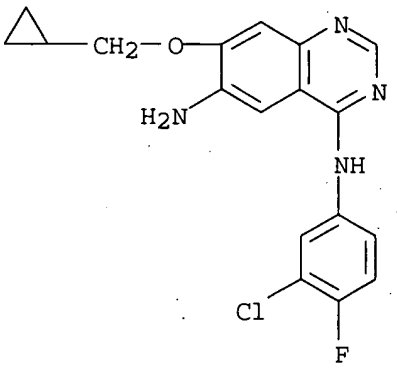
TI Preparation of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction.
IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PA Boehringer Ingelheim Pharma K.-G., Germany
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
	DE 10017539	A1	20011011	DE 2000-10017539	20000408
	DE 10040525	A1	20020228	DE 2000-10040525	20000818
	EP 1280798	A1	20030205	EP 2001-938076	20010331
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
				WO 2001-EP3694 W	20010331

PATENT FAMILY INFORMATION:
FAN 2001:747043

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10017539	A1	20011011	DE 2000-10017539	20000408
	US 2001044435	A1	20011122	US 2001-816003	20010323
				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
	WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
	EP 1280798	A1	20030205	EP 2001-938076	20010331
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
				WO 2001-EP3694 W	20010331

OS MARPAT 135:303907
IT **290304-07-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)
RN 290304-07-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



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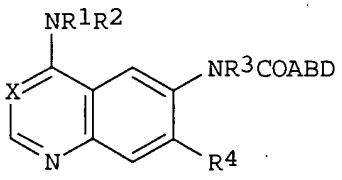

I

AB Title compds. [I; X = NCN, N; R1 = H, alkyl; R2 = (substituted) Ph, PhCH2, PhCH2CH2; R3 = H, alkyl; R4 = H, alkoxy, cycloalkoxy, cycloalkylalkoxy; A = (substituted) vinylene; B = bond, (fluoro)alkylene; D = substituted pyrrolidinyl, piperidinyl, piperazinyl, etc.], were prepd. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-(piperazin-1-yl)-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline (prepn. given) in THF was treated with Et3N and then with 3-bromodihydrofuran-2-one in THF under ice cooling followed by stirring for 48 h at room temp. to give 56% 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-[4-(2-oxotetrahydrofuran-3-yl)piperazin-1-yl]-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.05 nM.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2001:747043 CAPLUS
DN 135:303901
TI Bicyclic heterocycles as inhibitors of epidermal growth factor receptor

mediated signal transduction
IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PA Boehringer Ingelheim Pharma KG, Germany
SO Ger. Offen., 28 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10017539	A1	20011011	DE 2000-10017539	20000408
	US 2001044435	A1	20011122	US 2001-816003	20010323
				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
	WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
	EP 1280798	A1	20030205	EP 2001-938076	20010331
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				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
				WO 2001-EP3694 W	20010331

PATENT FAMILY INFORMATION:
FAN 2001:762992

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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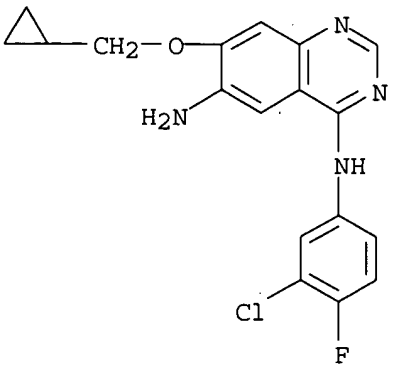
				DE 2000-10040525A	20000818
	DE 10017539	A1	20011011	DE 2000-10017539	20000408
	DE 10040525	A1	20020228	DE 2000-10040525	20000818
	EP 1280798	A1	20030205	EP 2001-938076	20010331
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
				DE 2000-10017539A	20000408
				DE 2000-10040525A	20000818
				WO 2001-EP3694 W	20010331

OS MARPAT 135:303901

IT **290304-07-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)
RN 290304-07-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



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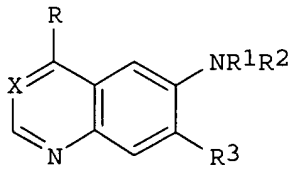

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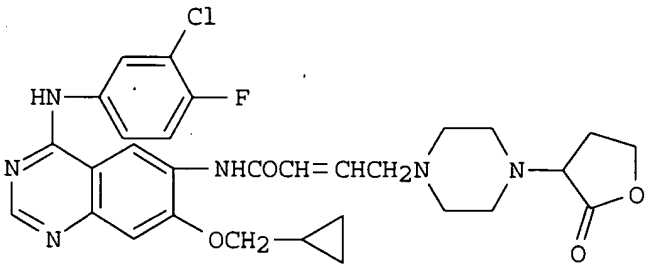


II

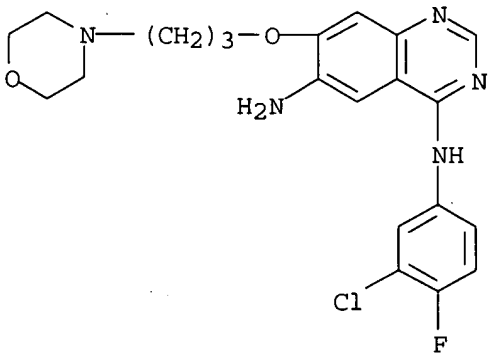
AB Bicyclic heterocycles I [X = N, CCN; R = substituted NH2; R1 = H, alkyl; R2 = acyl; R3 = H, (un)substituted alkoxy, cycloalkoxy, tetrahydrofuranyloxy, tetrahydropyranyloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy] were prepd. for use as inhibitors of tyrosine kinase-mediated signal transduction for treatment of tumors and diseases of the lung and airway. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-7-fluoro-6-nitroquinazoline was treated with cyclopropylmethanol, followed by redn. to the amine, reaction with 4-bromocrotonic acid and N-tert.-

butoxycarbonylpiperazine, and deblocking to give the quinazoline II. II had an IC50 for inhibition of epidermal growth factor dependent proliferation of 0.05 nM.

L4 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2001:636060 CAPLUS
DN 135:211054
TI Method for the simplified production of N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-nitroquinazolin-4-yl]amine or N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-aminoquinazolin-4-yl]-amine
IN Barth, Hubert; Steiner, Klaus; Schneider, Simon
PA Goedecke G.m.b.H., Germany
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001062743	A2	20010830	WO 2001-EP695	20010123
WO 2001062743	A3	20020314		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
			DE 2000-10009267A	20000226
DE 10009267	A1	20010830	DE 2000-10009267	20000226
BR 2001008695	A	20021210	BR 2001-8695	20010123
			DE 2000-10009267A	20000226
			WO 2001-EP695 W	20010123
EP 1265874	A2	20021218	EP 2001-953631	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
			DE 2000-10009267A	20000226
			WO 2001-EP695 W	20010123
US 2003050313	A1	20030313	US 2002-204911	20020826
			DE 2000-10009267A	20000226
			WO 2001-EP695 W	20010123

OS CASREACT 135:211054
IT **267243-68-5P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(method for the simplified prodn. of N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-nitroquinazolin-4-yl]amine or N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-aminoquinazolin-4-yl]-amine)
RN 267243-68-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



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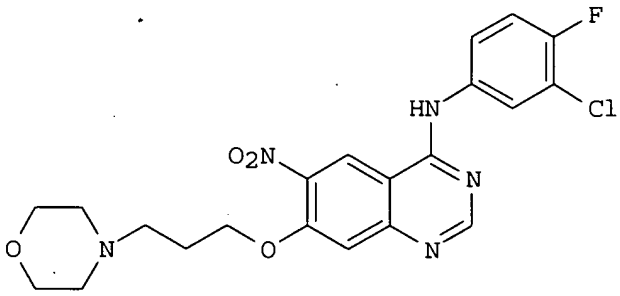

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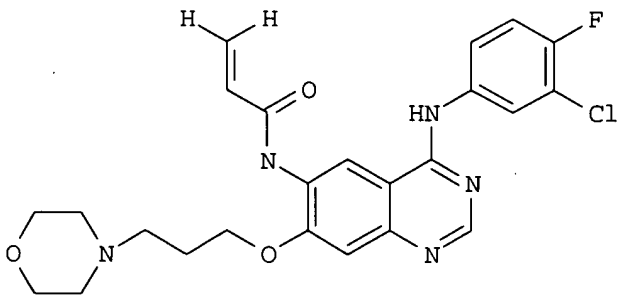


II

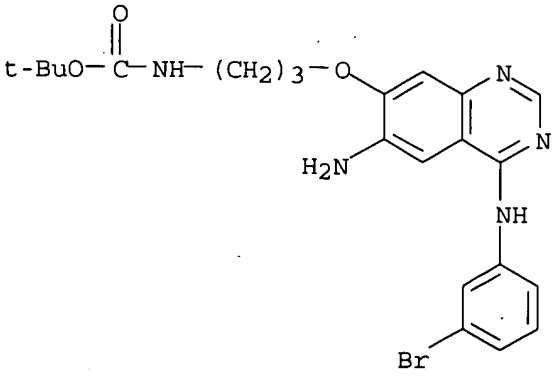
AB N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-nitroquinazolin-4-yl]amine (I) or N-(3-chloro-4-fluorophenyl)-N-[7-[3-(4-morpholinyl)propoxy]-6-aminoquinazolin-4-yl]amine (II) are prepd. in high yield and selectivity by the chlorination of 7-fluoro-6-nitroquinazolin-4(3H)-one with thionyl chloride to give 4-chloro-7-fluoro-6-nitroquinazoline which is condensed with 3-(4-morpholinyl)-1-propanol to give I which is then hydrogenated (e.g., using Raney nickel) into II.

L4 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2001:380438 CAPLUS
DN 135:24657
TI Selective cellular targeting: multifunctional delivery vehicles
IN Glazier, Arnold
PA Drug Innovation + Design, Inc., USA

SO PCT Int. Appl., 981 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001036003	A2	20010525	WO 2000-US31262	20001114
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
			US 1999-165485PP	19991115
			US 2000-239478PP	20001011
			US 2000-241937PP	20001020
AU 2001016075	A5	20010530	AU 2001-16075	20001114
			US 1999-165485PP	19991115
			US 2000-239478PP	20001011
			US 2000-241937PP	20001020
			WO 2000-US31262W	20001114
EP 1255567	A1	20021113	EP 2000-978631	20001114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
			US 1999-165485PP	19991115
			US 2000-239478PP	20001011
			US 2000-241937PP	20001020
			WO 2000-US31262W	20001114

IT **341551-80-2P**
RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(multifunctional delivery vehicles for selective cellular targeting of drugs)
RN 341551-80-2 CAPLUS
CN Carbamic acid, [3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



AB The present invention relates to the compns., methods, and applications of a novel approach to selective cellular targeting. The purpose of this invention is to enable the selective delivery and/or selective activation of effector mols. to target cells for diagnostic or therapeutic purposes. The present invention relates to multi-functional prodrugs or targeting vehicles wherein each functionality is capable of enhancing targeting selectivity, affinity, intracellular transport, activation or detoxification. The present invention also relates to ultralow dose, multiple target, multiple drug chemotherapy and targeted immunotherapy for cancer treatment.

L4 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2000:911231 CAPLUS
DN 134:71599
TI Preparation of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors.
IN Himmelsbach, Frank; Langkopf, Elke; Metz, Thomas; Solca, Flavio; Jung, Birgit; Baum, Anke
PA Boehringer Ingelheim Pharma K.-G., Germany
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000078735	A1	20001228	WO 2000-EP5547	20000616
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				DE 1999-19928281A	19990621
				US 1999-146644PP	19990730
				DE 2000-10023085A	20000511
	DE 19928281	A1	20001228	DE 1999-19928281	19990621
	DE 10023085	A1	20011115	DE 2000-10023085	20000511
	BR 2000011834	A	20020312	BR 2000-11834	20000616
				DE 1999-19928281A	19990621
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				WO 2000-EP5547 W	20000616
	EP 1194418	A1	20020410	EP 2000-936888	20000616
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				DE 1999-19928281A	19990621
				US 1999-146644PP	19990730
				DE 2000-10023085A	20000511
				WO 2000-EP5547 W	20000616
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			WO 2000-EP5547 W 20000616
BG 106189	A	20020830	BG 2001-106189 20011207
			DE 1999-19928281A 19990621
			US 1999-146644PP 19990730
			DE 2000-10023085A 20000511
			WO 2000-EP5547 W 20000616
US 2002169180	A1	20021114	US 2001-16280 20011210
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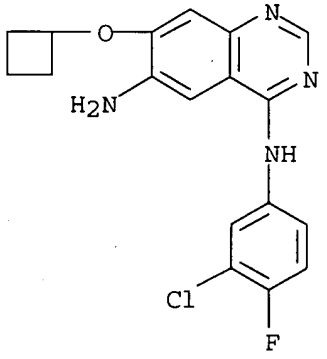
			US 1999-146644PP 19990730
			DE 2000-10023085A 20000511
NO 2001006185	A	20011218	NO 2001-6185 20011218
			DE 1999-19928281A 19990621
			US 1999-146644PP 19990730
			DE 2000-10023085A 20000511
			WO 2000-EP5547 W 20000616

OS MARPAT 134:71599

IT **290303-28-5P 290303-32-1P 290304-07-3P**
314771-70-5P 314771-71-6P 314771-72-7P
314771-73-8P 314771-74-9P 314771-75-0P
314771-76-1P 314771-77-2P 314771-80-7P
314771-81-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors)

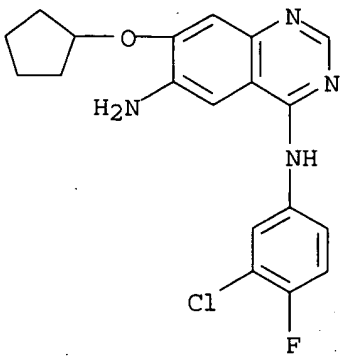
RN 290303-28-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclobutyloxy)- (9CI) (CA INDEX NAME)

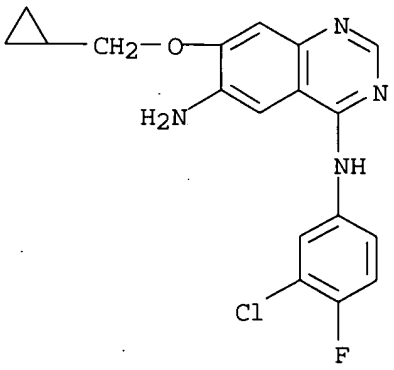


RN 290303-32-1 CAPLUS

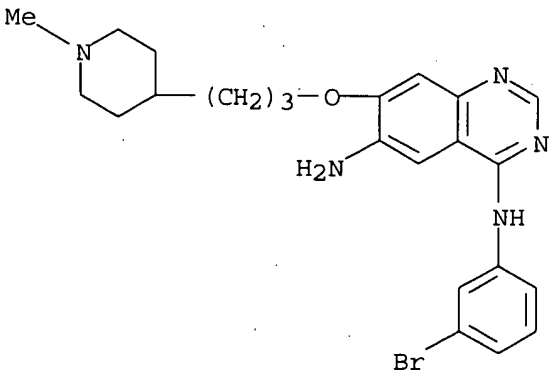
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopentyloxy)- (9CI) (CA INDEX NAME)



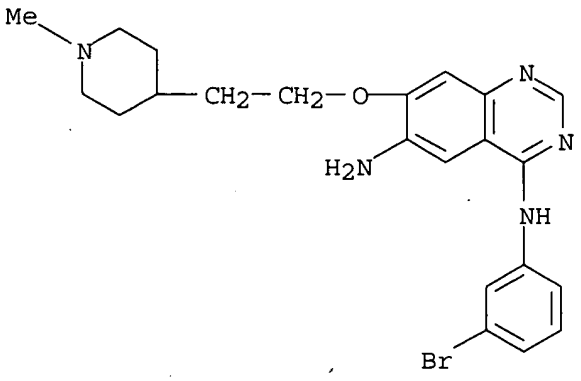
RN 290304-07-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopropylmethoxy)- (9CI) (CA INDEX NAME)



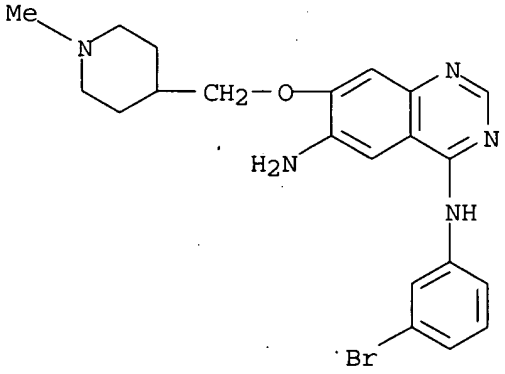
RN 314771-70-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(1-methyl-4-piperidinyl)propoxy]- (9CI) (CA INDEX NAME)



RN 314771-71-6 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[2-(1-methyl-4-piperidinyl)ethoxy]- (9CI) (CA INDEX NAME)



RN 314771-72-7 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[(1-methyl-4-piperidinyl)methoxy]- (9CI) (CA INDEX NAME)



RN 314771-73-8 CAPLUS
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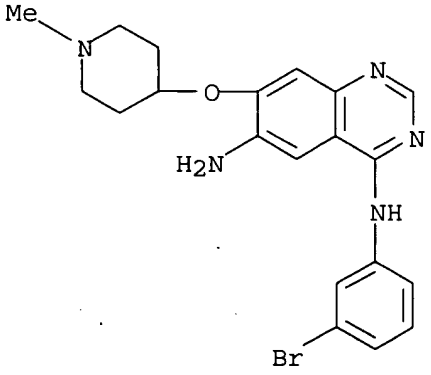

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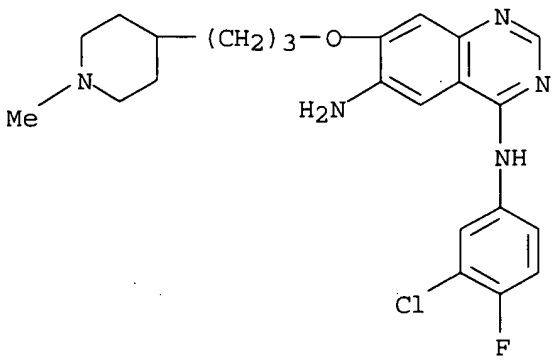

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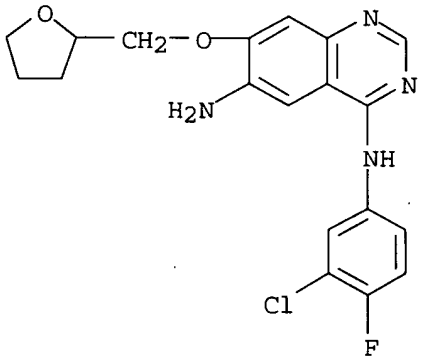
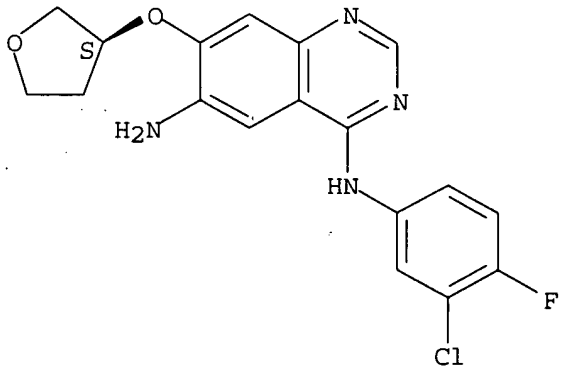


RN 314771-76-1 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[[(3S)-tetrahydro-3-furanyl]oxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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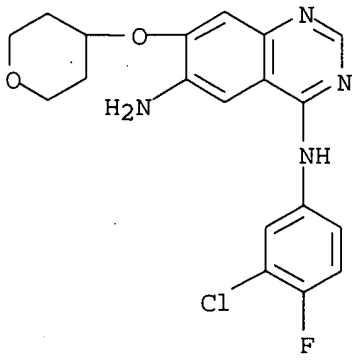

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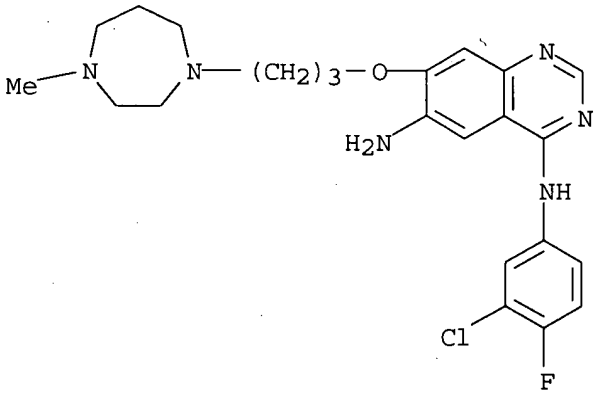

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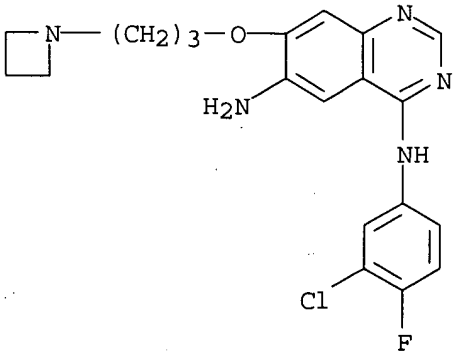

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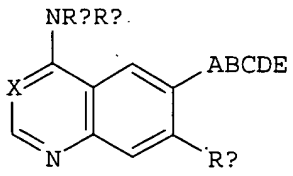

I

AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH2, PhCH2CH2; Rc = (substituted) cycloalkoxy, cycloalkylalkoxy; A = (alkyl-substituted) imino; B = CO, SO2; C = (substituted) allenylene, vinylene, butadienylene, ethynylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, carbonyloxyalkylene, carbonyliminoalkylene, bond, etc.; E = amino, (substituted) alkylamino, dialkylamino, etc.], were prepd. Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propoxy]quinazoline (prepn. given) in CH2Cl2 contg. Et3N at -10.degree. was treated with acryloyl chloride in THF to give 35% 4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation of F/L HERC cells with IC50 = <0.35 nM.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2000:628125 CAPLUS
DN 133:207919
TI Preparation of 4-amino-quinazoline and quinoline derivatives having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases
IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas; Solca, Flavio; Blech, Stefan
PA Boehringer Ingelheim Pharma K.-G., Germany
SO PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000051991	A1	20000908	WO 2000-EP1496	20000224

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PATENT FAMILY INFORMATION:

FAN 2000:607393

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OS MARPAT 133:207919

IT **153437-17-3 290304-06-2 290304-07-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

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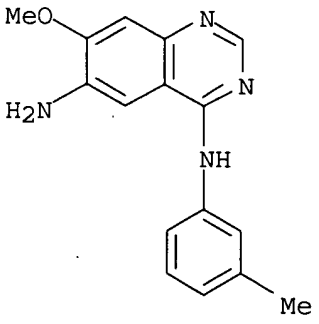
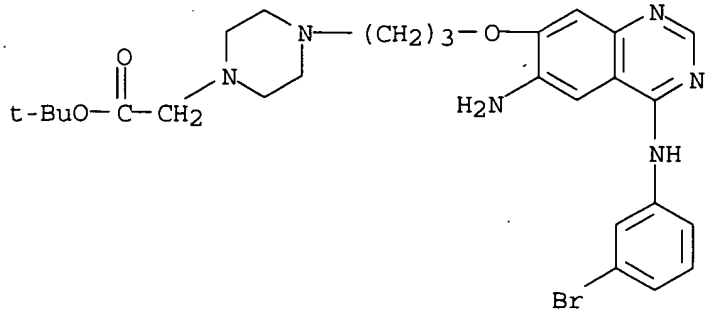
CN 4,6-Quinazolinediamine, 7-methoxy-N4-(3-methylphenyl)- (9CI) (CA INDEX NAME)



RN 290304-06-2 CAPLUS

CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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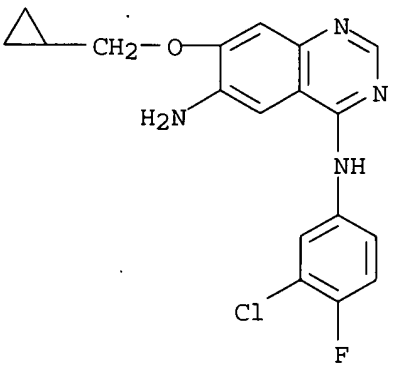

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(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 289700-72-7 CAPLUS
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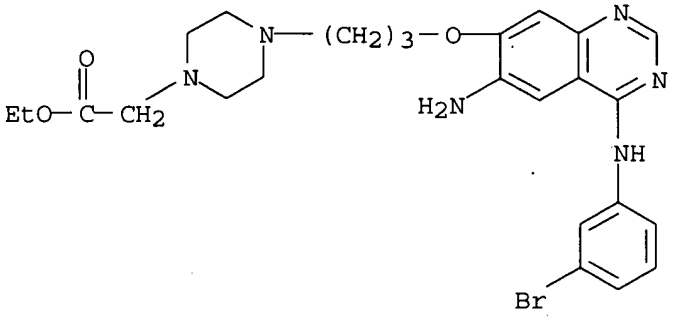

RN 289700-73-8 CAPLUS
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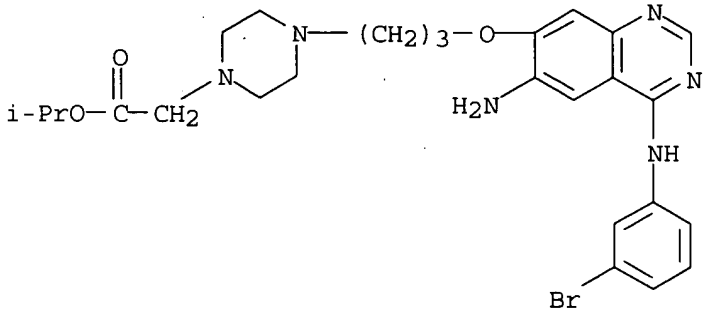

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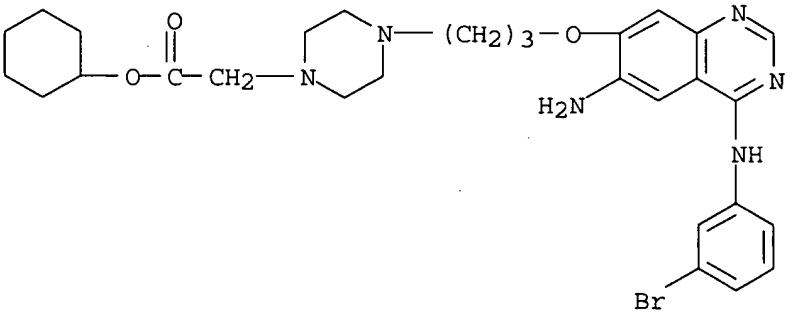
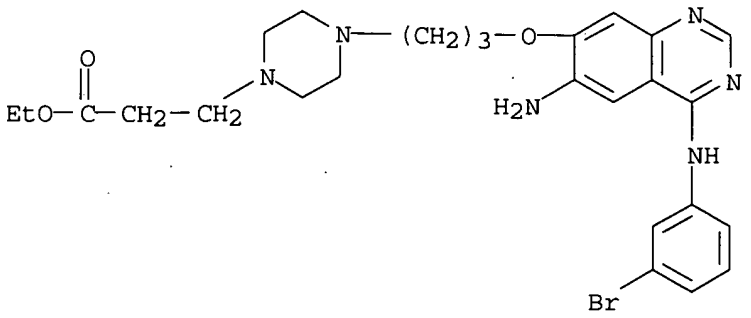
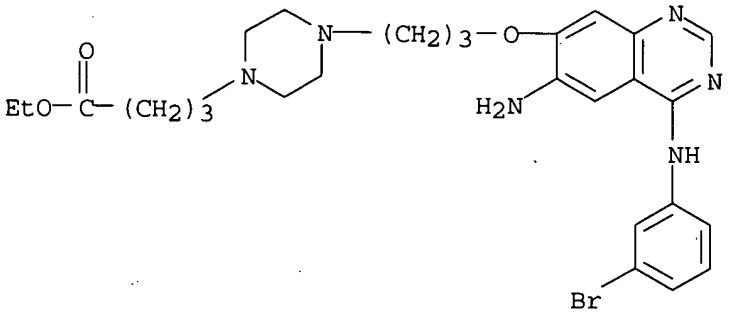


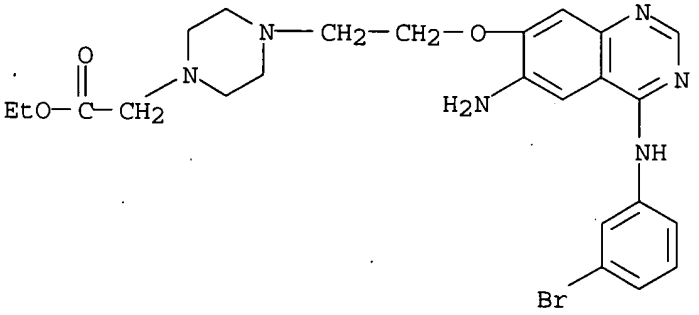
RN 289700-75-0 CAPLUS
CN 1-Piperazinepropanoic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 289700-76-1 CAPLUS
CN 1-Piperazinebutanoic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 289700-77-2 CAPLUS
CN 1-Piperazineacetic acid, 4-[2-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 289700-78-3 CAPLUS
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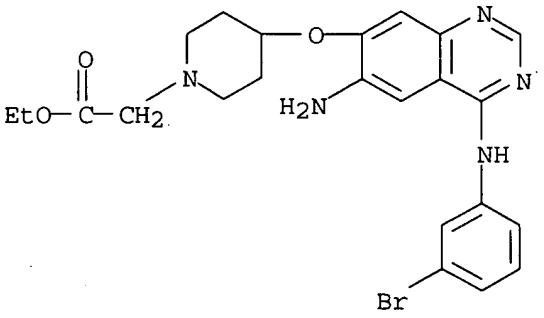

RN 289700-79-4 CAPLUS
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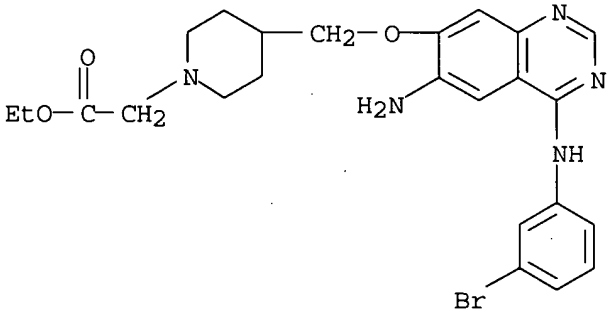

RN 289700-80-7 CAPLUS
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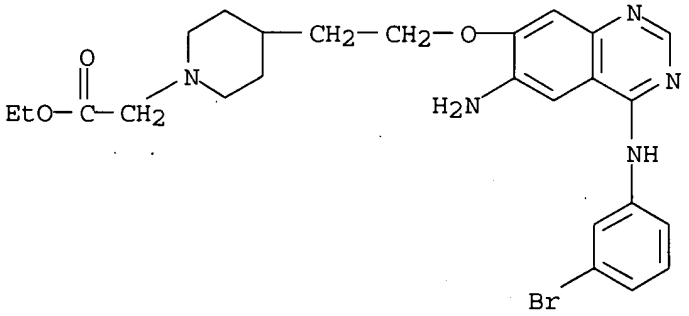

RN 289700-81-8 CAPLUS
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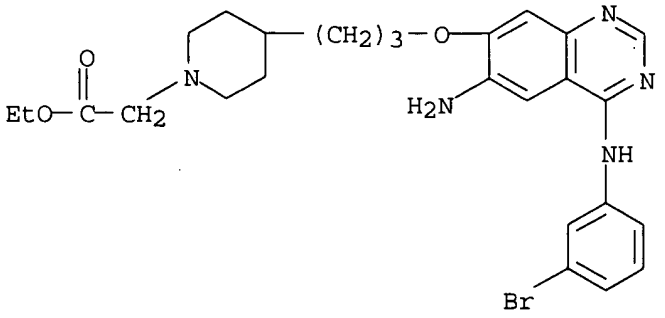
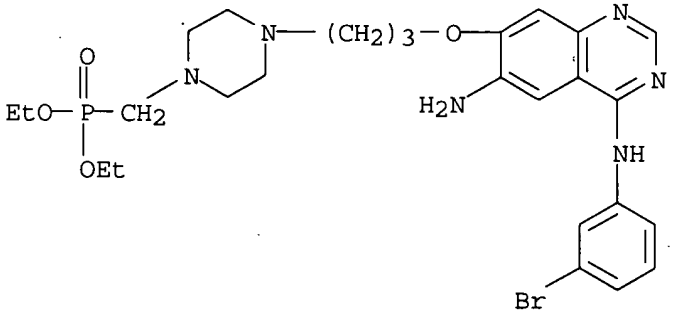
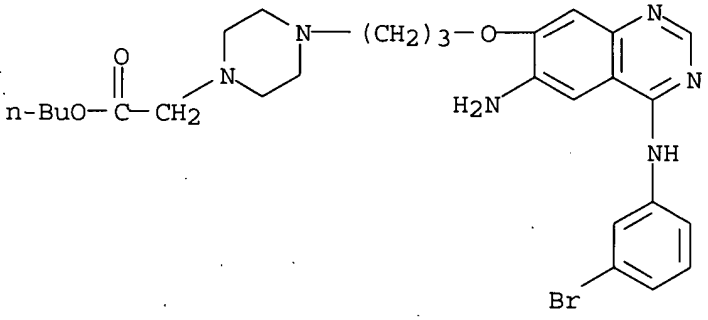


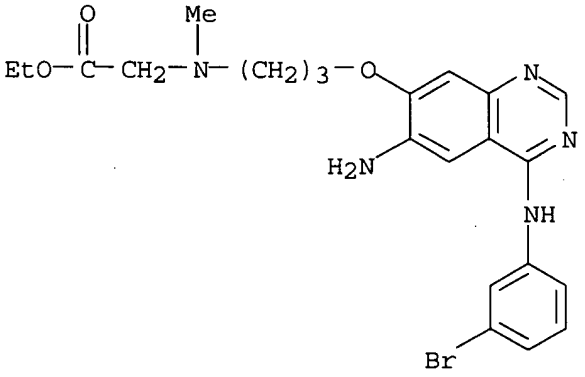
RN 290303-20-7 CAPLUS
CN Phosphonic acid, [[4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-1-piperazinyl]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



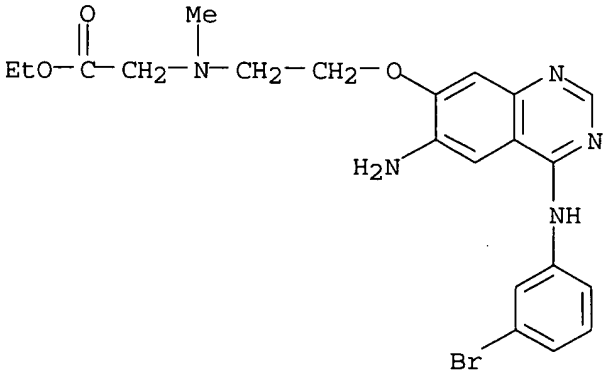
RN 290303-21-8 CAPLUS
CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, butyl ester (9CI) (CA INDEX NAME)



RN 290303-22-9 CAPLUS
CN Glycine, N-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 290303-23-0 CAPLUS
CN Glycine, N-[2-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]ethyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



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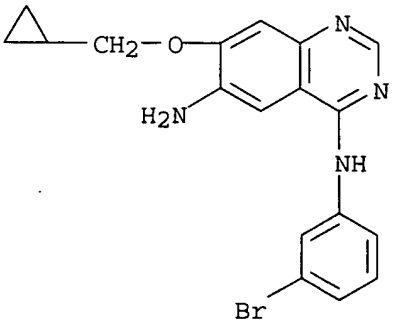

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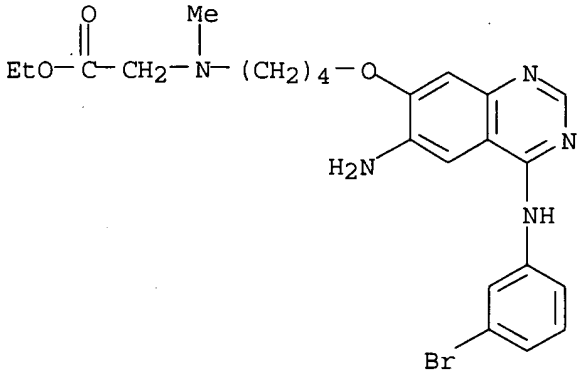
CN Glycine, N-[4-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]butyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



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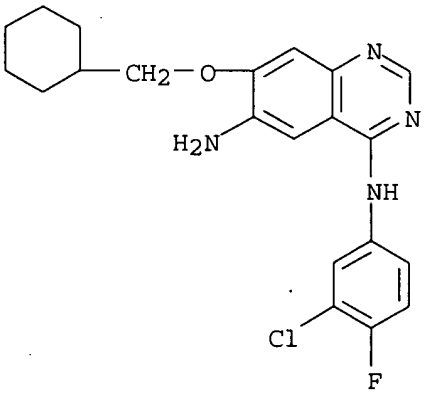
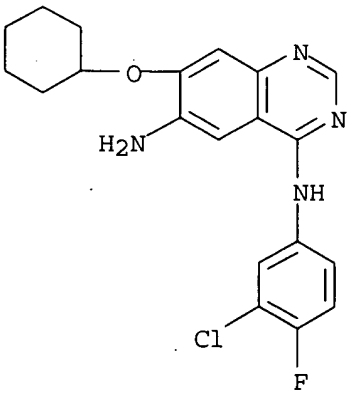
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclohexylmethoxy)-
(9CI) (CA INDEX NAME)

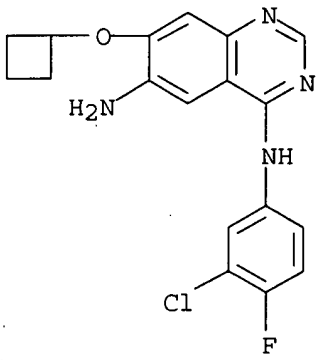


RN 290303-27-4 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclohexyloxy)-
(9CI) (CA INDEX NAME)



RN 290303-28-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclobutyloxy)-
(9CI) (CA INDEX NAME)



RN 290303-29-6 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclobutylmethoxy)-
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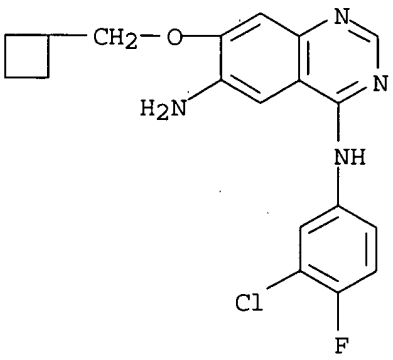

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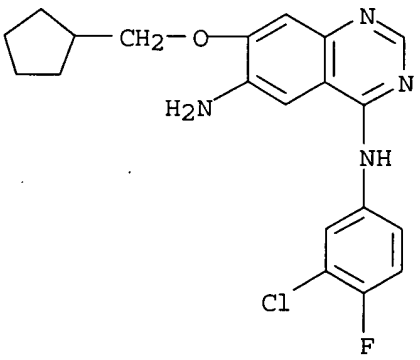
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-
(cyclopentylmethoxy)- (9CI) (CA INDEX NAME)



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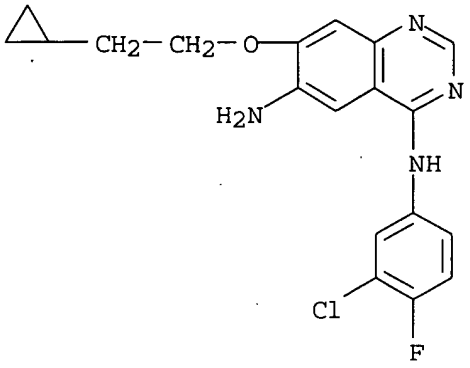
cyclopropylethoxy)- (9CI) (CA INDEX NAME)



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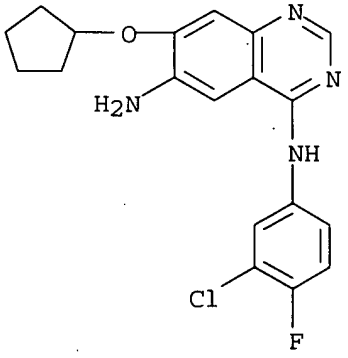
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-(cyclopentyloxy)- (9CI) (CA INDEX NAME)



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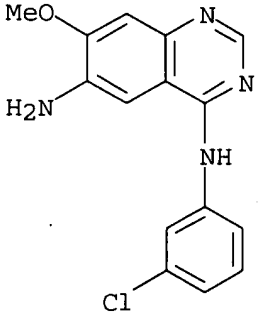
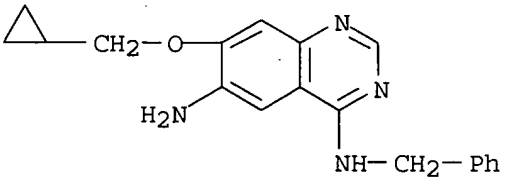
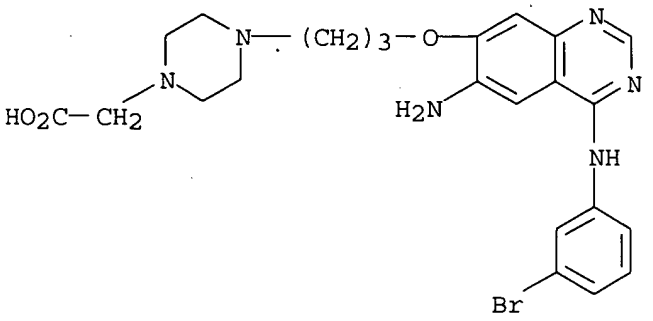
CN 4,6-Quinazolinediamine, N4-(3-chlorophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



RN 290303-44-5 CAPLUS
CN 4,6-Quinazolinediamine, 7-(cyclopropylmethoxy)-N4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 290303-73-0 CAPLUS
CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]- (9CI) (CA INDEX NAME)



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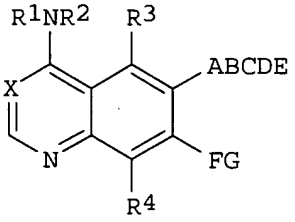

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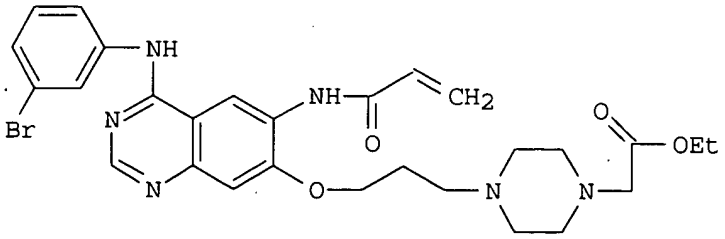

II

AB Title compds. [I; R1 = H, C1-C4-alkyl; R2 = (un)substituted Ph, benzyl, 1-phenylethyl; R3, R4 independently = H, F, Cl, CH3O, CH3OCH2, (CH3)2NCH2, (CH3CH2)2NCH2, pyrrolidino, piperidino, morpholino; X = C(CN), N; A = O, NH, (C1-C4)-alkylN; B = CO, SO2; C = 1,3-allenylene, 1,1-vinylene, 1,2-vinylene, 1,3-butadien-1,4-ylene, with CH3, CF3 substitution; D = alkylene, CO-alkylene, SO2-alkylene; CO, SO2; E = HOCO(CH2)nNR5, (HO)2P(:O)(CH2)nNR5; n = 1-6; R5 = H, alkyl], tautomers, stereoisomers, and physiol. acceptable salts are prepd. and having valuable pharmacol. properties, particularly an inhibiting effect on signal transduction mediated by tyrosine kinases. Title compds. are useful for treating tumoral diseases, diseases of the lungs and respiratory tract. Thus, the title compd. II was prepd. and tested by Cell Titer 96TM Aq. Nonradioactive Cell Proliferation Assay.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2000:607393 CAPLUS
DN 133:207916
TI Preparation of aminoquinazolines as epidermal growth factor receptor inhibitors.
IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas
PA Boehringer Ingelheim Pharma K-G, Germany
SO Ger. Offen., 26 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

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PATENT FAMILY INFORMATION:

FAN 2000:628125

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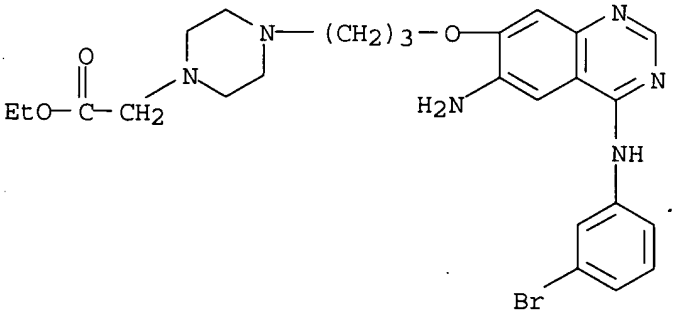
OS MARPAT 133:207916

IT **289700-72-7P 289700-73-8P 289700-74-9P**
289700-75-0P 289700-76-1P 289700-77-2P
289700-78-3P 289700-79-4P 289700-80-7P
289700-81-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of aminoquinazolines as epidermal growth factor receptor inhibitors)

RN 289700-72-7 CAPLUS

CN 1-Piperazineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 289700-73-8 CAPLUS

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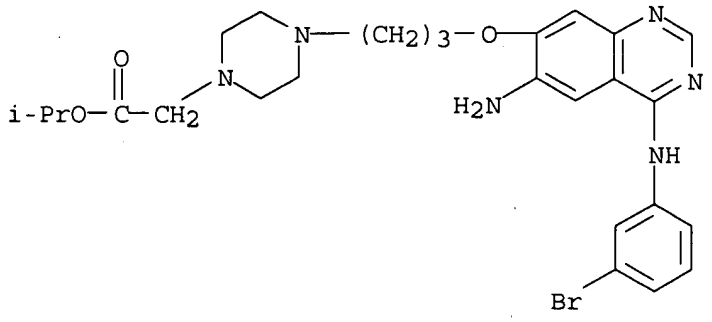

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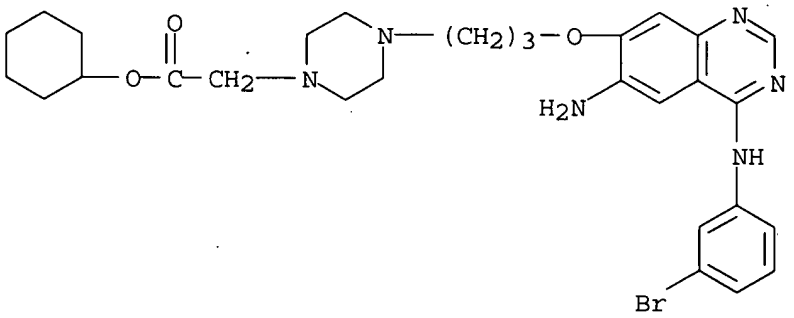

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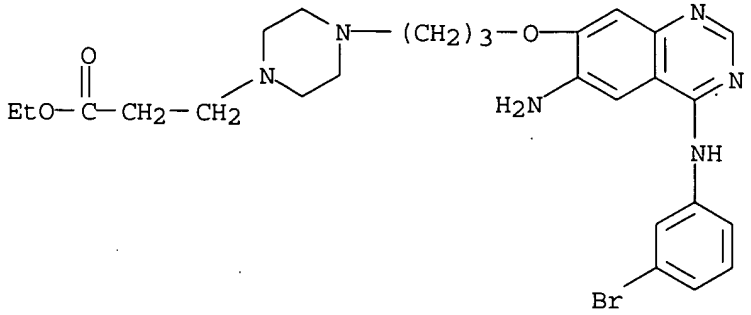

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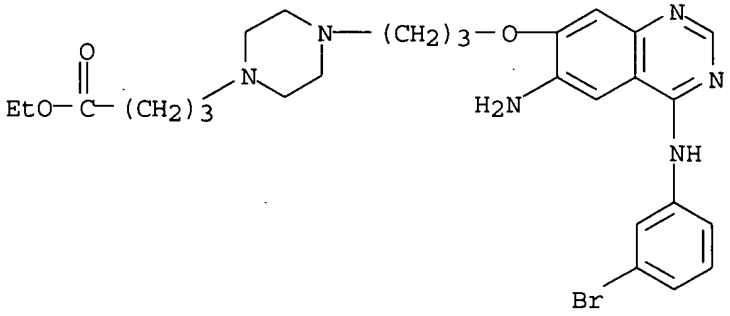

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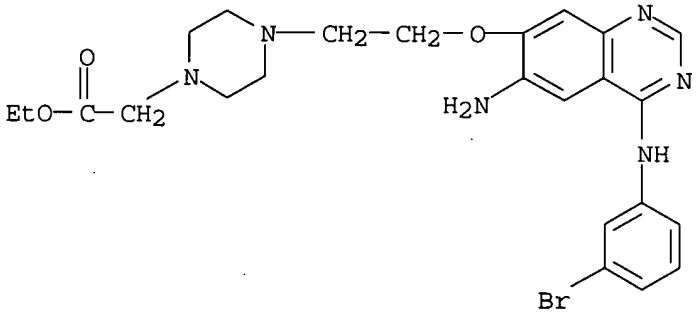
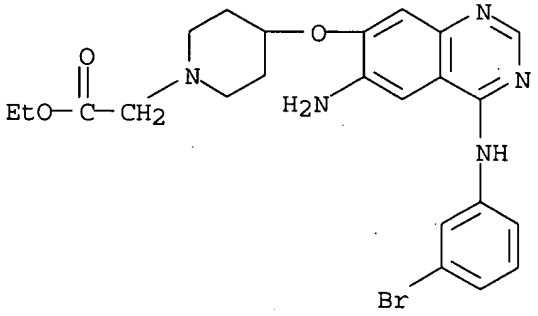
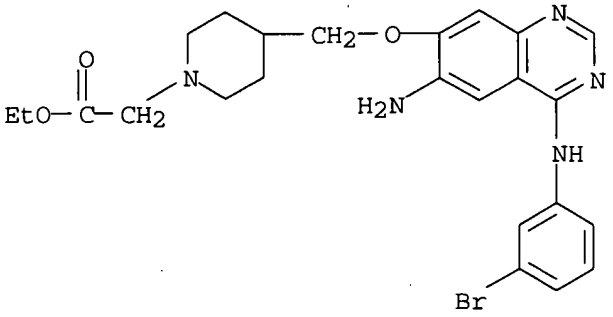


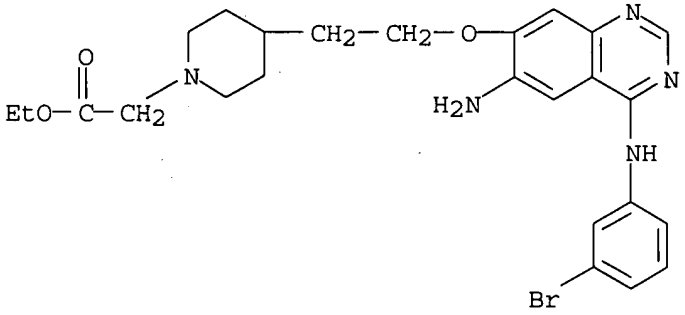
RN 289700-78-3 CAPLUS
CN 1-Piperidineacetic acid, 4-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]-, ethyl ester (9CI) (CA INDEX NAME)



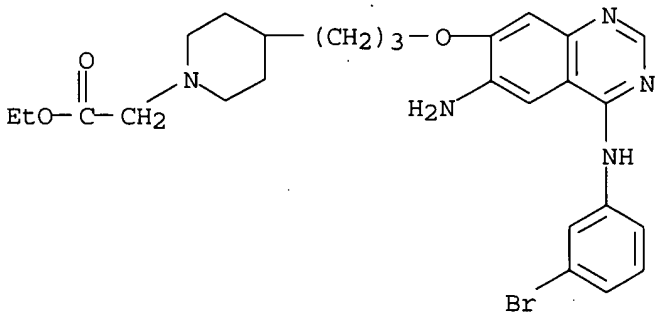
RN 289700-79-4 CAPLUS
CN 1-Piperidineacetic acid, 4-[[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]methyl]-, ethyl ester (9CI) (CA INDEX NAME)



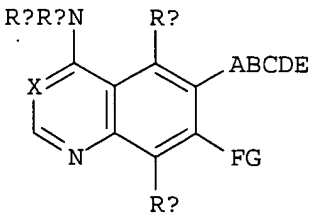
RN 289700-80-7 CAPLUS
CN 1-Piperidineacetic acid, 4-[2-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 289700-81-8 CAPLUS
CN 1-Piperidineacetic acid, 4-[3-[[6-amino-4-[(3-bromophenyl)amino]-7-quinazolinyl]oxy]propyl]-, ethyl ester (9CI) (CA INDEX NAME)



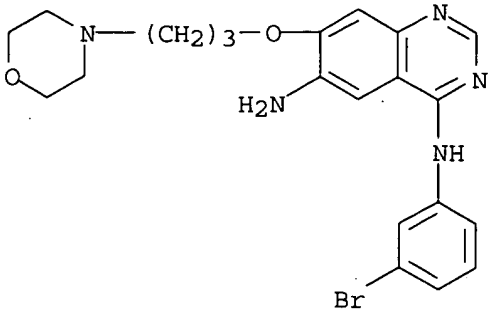
GI



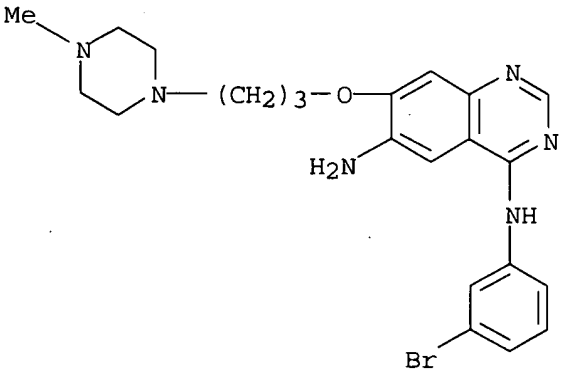
I

AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH2, 1-phenylethyl; Rc, Rm = H, F, Cl, MeO, (methoxy-, dimethylamino-, diethylamino-, pyrrolidino-, piperidino-, morpholino- substituted) Me; X = N, NCC; A = O, alkylimino; B = CO, SO2; C = (Me- or F3C-substituted) allenylene, vinylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, etc.; E, G = (substituted) R6O2CYNR5, etc.; R5 = H, (substituted) alkyl; R6 = H, (substituted) alkyl, cycloalkyl, alkenyl, alkynyl, etc.; F = alkylene, oxyalkylene, O; FG = H, F, Cl, alkoxy, etc.], were prepd. Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-[4-(ethoxycarbonyl)methylpiperazin-1-yl]propoxy]quinazoline (prepn. given) in CH2Cl2 contg. Et3N was treated with acryloyl chloride in CH2Cl2 at -10.degree. to give 62% 4-[(3-bromophenyl)amino]-7-[3-[4-[(ethoxycarbonyl)methyl]piperazin-1-yl]propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation with IC50 = 2.6 nM.

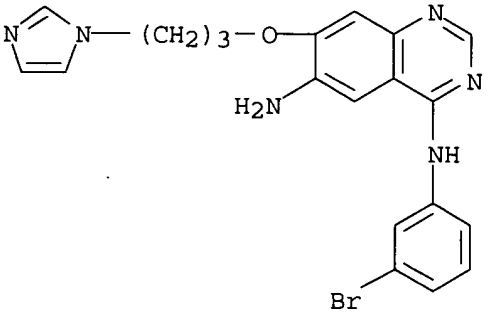
L4 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2000:481416 CAPLUS
DN 134:216784
TI Tyrosine kinase inhibitors. 17. Irreversible inhibitors of the epidermal growth factor receptor: 4-(phenylamino)quinazoline- and 4-(phenylamino)pyrido[3,2-d]pyrimidine-6-acrylamides bearing additional solubilizing functions. [Erratum to document cited in CA132:317628]
AU Smaill, Jeff B.; Rewcastle, Gordon W.; Bridges, Alexander J.; Zhou, Hairong; Showalter, H. D. Hollis; Fry, David W.; Nelson, James M.; Sherwood, Veronika; Elliott, William L.; Vincent, Patrick W.; DeJohn, Dana E.; Loo, Joseph A.; Greis, Kenneth D.; Chan, O. Helen; Reyner, Eric L.; Lipka, Elke; Denny, William A.
CS Auckland Cancer Society Research Centre, Faculty Medical and Health Sciences, The Univ. Auckland, Auckland, N. Z.
SO Journal of Medicinal Chemistry (2000), 43(16), 3199
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
IT **198961-78-3P 198961-84-1P 198961-86-3P 198961-87-4P 267243-67-4P 267243-68-5P 267243-69-6P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antitumor and EGFR enzyme-inhibiting SAR of quinazolines (Erratum))
RN 198961-78-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-morpholinyl)propoxy]-(9CI) (CA INDEX NAME)



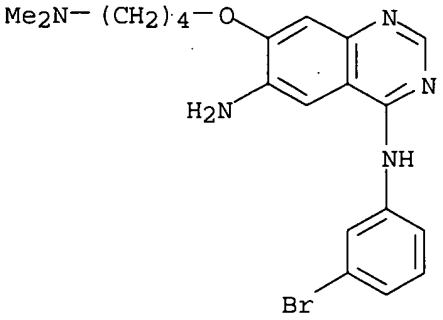
RN 198961-84-1 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)



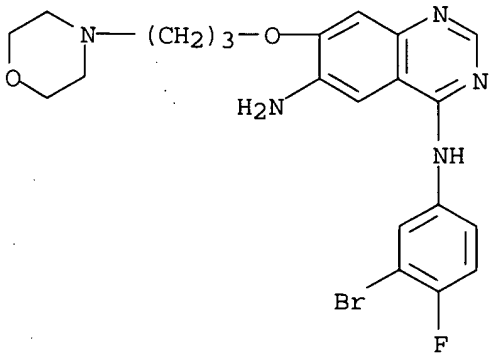
RN 198961-86-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(1H-imidazol-1-yl)propoxy]- (9CI) (CA INDEX NAME)



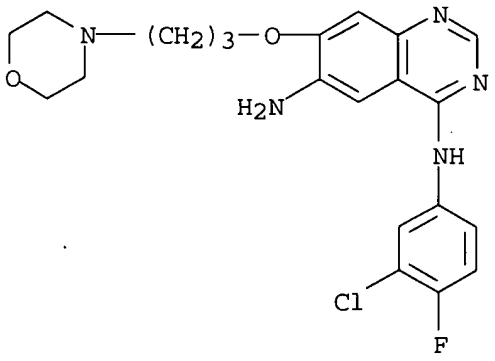
RN 198961-87-4 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[4-(dimethylamino)butoxy]- (9CI) (CA INDEX NAME)



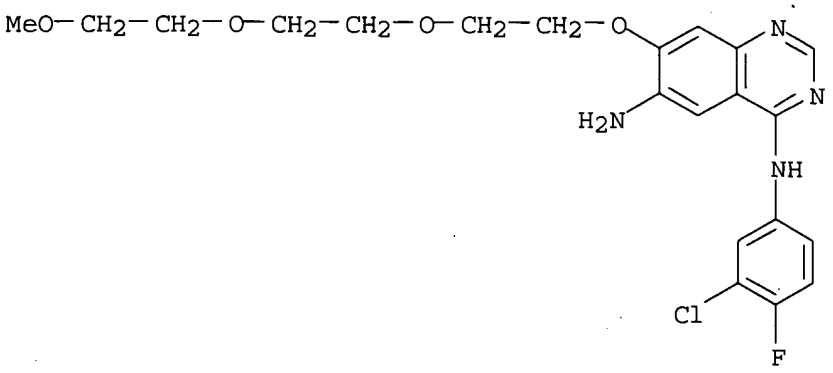
RN 267243-67-4 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromo-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



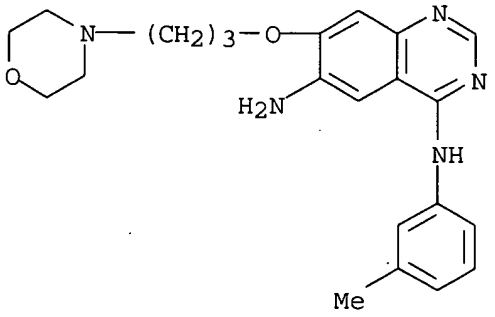
RN 267243-68-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



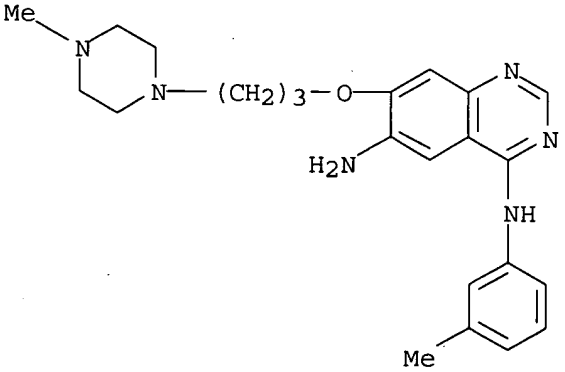
RN 267243-69-6 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[2-[2-(2-methoxyethoxy)ethoxy]ethoxy]- (9CI) (CA INDEX NAME)



IT **198961-80-7P 198961-82-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antitumor and EGFR enzyme-inhibiting SAR of quinazolines (Erratum))
RN 198961-80-7 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



RN 198961-82-9 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)



AB Six author names were inadvertently omitted from the author contribution

line. The complete author list is as follows: Jeff B. Smaill, Gordon W. Rewcastle, Alexander J. Bridges, Hairong Zhou, H. D. Hollis Showalter, David W. Fry, James M. Nelson, Veronika Sherwood, William L. Elliott, Patrick W. Vincent, Dana E. DeJohn, Joseph A. Loo, Kenneth D. Greis, O. Helen Chan, Eric L. Reyner, Elke Lipka, and William A. Denny.

L4 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2000:368316 CAPLUS
DN 133:4672
TI Preparation of N-{4-(3-chloro-4-fluorophenylamino)-7-[3-(morpholin-4-yl)propoxy]quinazolin-6-yl}acrylamide as an irreversible inhibitor of tyrosine kinases
IN Bridges, Alexander James; Driscoll, Denise; Klohs, Wayne Daniel
PA Warner-Lambert Co., USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000031048	A1	20000602	WO 1999-US22116	19990923
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	AU 9962612	A1	20000613	AU 1999-62612	19990923
				US 1998-109065PP	19981119
				WO 1999-US22116W	19990923
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				US 1998-109065PP	19981119
				WO 1999-US22116W	19990923
	EE 200100271	A	20021015	EE 2001-271	19990923
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				WO 1999-US22116W	19990923
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				US 1998-109065PP	19981119
				WO 1999-US22116W	19990923
	US 6344455	B1	20020205	US 2001-831991	20010516
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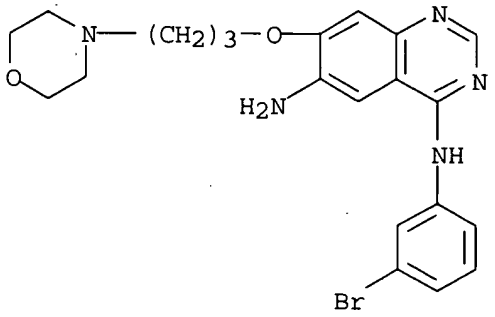
				WO 1999-US22116W	19990923
	NO 2001002465	A	20010713	NO 2001-2465	20010518
				US 1998-109065PP	19981119
				WO 1999-US22116W	19990923
	BG 105608	A	20020131	BG 2001-105608	20010615

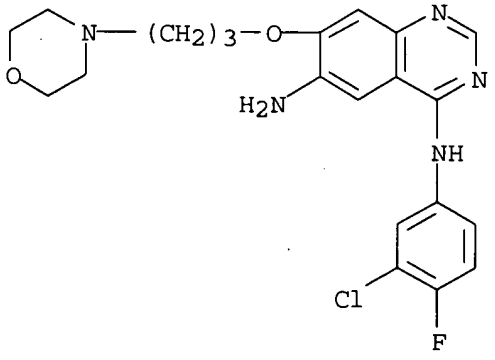
US 1998-109065PP 19981119
WO 1999-US22116W 19990923

IT **198961-78-3P 267243-68-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-{4-(3-chloro-4-fluorophenylamino)-7-[3-(morpholin-4-yl)propoxy]quinazolin-6-yl}acrylamide as an irreversible inhibitor of tyrosine kinases)

RN 198961-78-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-morpholinyl)propoxy]-(9CI) (CA INDEX NAME)



RN 267243-68-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



AB The title compd. that is an irreversible inhibitor of tyrosine kinases such as EGFR, erbB2, and erbB4, and inhibitor of the tyrosine phosphorylation of erbB3 and VEGF secretion (biol. data were given), was prepd. The title compd. is useful in treating cancer, restenosis, atherosclerosis, endometriosis, and psoriasis.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 2000:164843 CAPLUS
DN 132:317628
TI Tyrosine kinase inhibitors. 17. Irreversible inhibitors of the epidermal growth factor receptor: 4-(Phenylamino)quinazoline- and

4-(Phenylamino)pyrido[3,2-d]pyrimidine-6-acrylamides bearing additional solubilizing functions

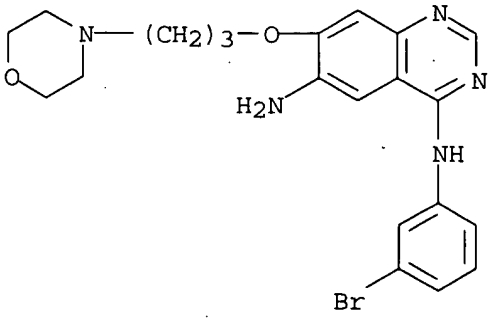
AU Smaill, Jeff B.; Rewcastle, Gordon W.; Loo, Joseph A.; Greis, Kenneth D.; Chan, O. Helen; Reyner, Eric L.; Lipka, Elke; Showalter, H. D. Hollis; Vincent, Patrick W.; Elliott, William L.; Denny, William A.

CS Auckland Cancer Society Research Centre Faculty of Medical and Health Sciences, The University of Auckland, Auckland, N. Z.

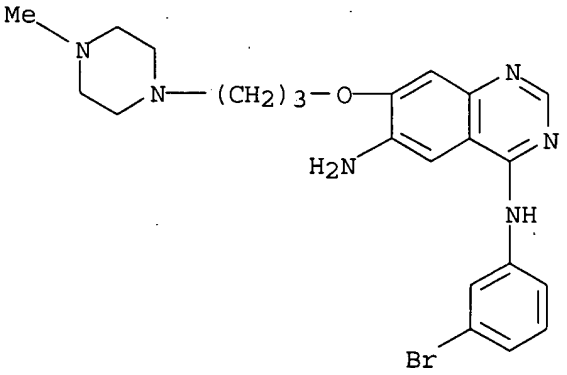
SO Journal of Medicinal Chemistry (2000), 43(7), 1380-1397
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English

IT **198961-78-3P 198961-84-1P 198961-86-3P 198961-87-4P 267243-67-4P 267243-68-5P 267243-69-6P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antitumor and EGFR enzyme-inhibiting SAR of quinazolines)

RN 198961-78-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)

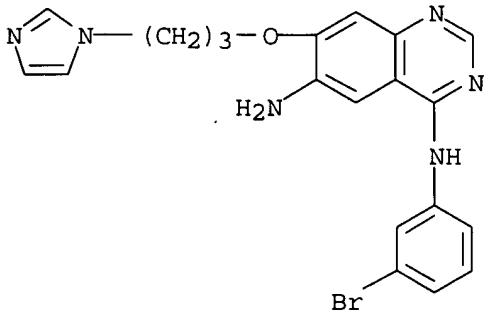


RN 198961-84-1 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)

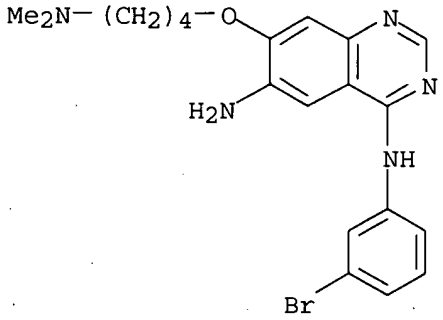


RN 198961-86-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(1H-imidazol-1-yl)propoxy]-

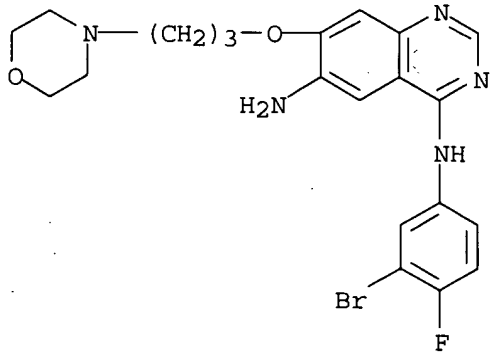
(9CI) (CA INDEX NAME)



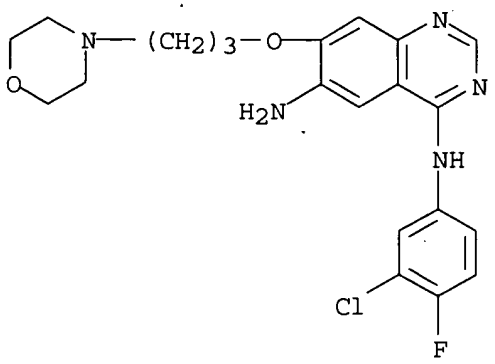
RN 198961-87-4 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[4-(dimethylamino)butoxy]- (9CI) (CA INDEX NAME)



RN 267243-67-4 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromo-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



RN 267243-68-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



RN 267243-69-6 CAPLUS
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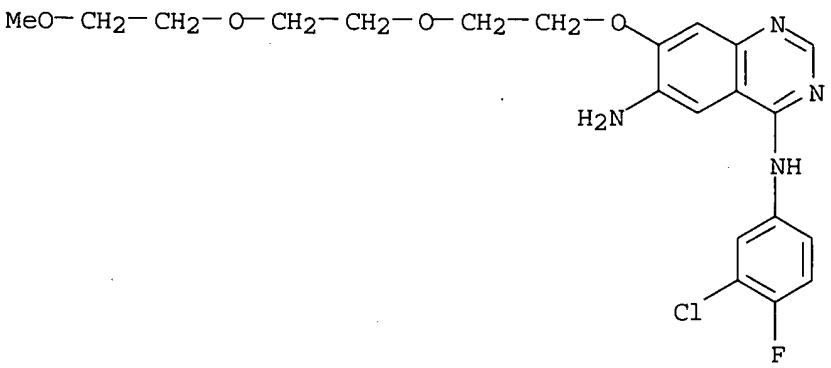
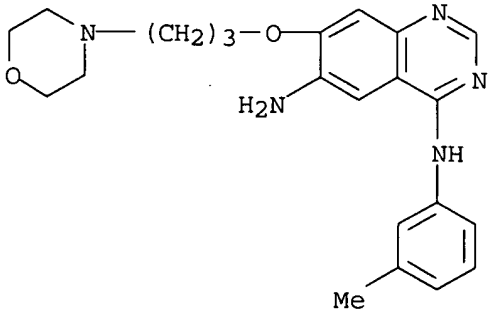
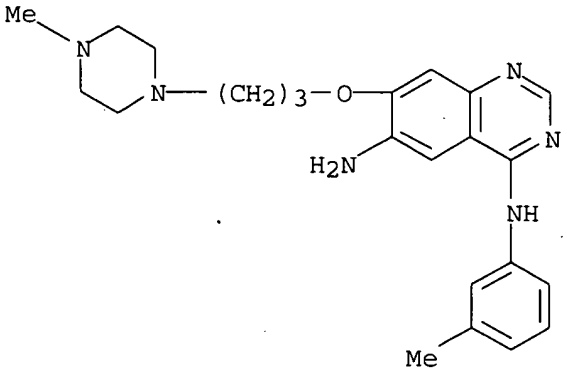


IT **198961-80-7P 198961-82-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antitumor and EGFR enzyme-inhibiting SAR of quinazolines)
RN 198961-80-7 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



RN 198961-82-9 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-methyl-1-

piperazinyl)propoxy]- (9CI) (CA INDEX NAME)

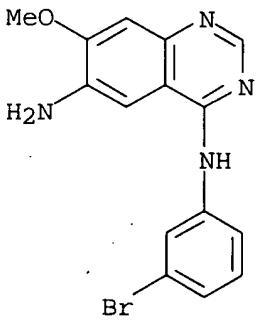


AB 4-Anilinoquinazoline- and 4-anilinopyrido[3,2-d]pyrimidine-6-acrylamides substituted with solubilizing 7-alkylamine or 7-alkoxyamine side chains were prepd. by reaction of the corresponding 6-amines with acrylic acid or acrylic acid anhydrides. In the pyrido[3,2-d]pyrimidine series, the intermediate 6-amino-7-alkylamines were prepd. from 7-bromo-6-fluoropyrido[3,2-d]pyrimidine via Stille coupling with the appropriate stannane under palladium(0) catalysis. This proved a versatile method for the introduction of cationic solubilizing side chains. The compds. were evaluated for their inhibition of phosphorylation of the isolated EGFR enzyme and for inhibition of EGF-stimulated autophosphorylation of EGFR in A431 cells and of heregulin-stimulated autophosphorylation of erbB2 in MDA-MB 453 cells. Quinazoline analogs with 7-alkoxyamine solubilizing groups were potent irreversible inhibitors of the isolated EGFR enzyme, with IC50[app] values from 2 to 4 nM, and potently inhibited both EGFR and erbB2 autophosphorylation in cells. 7-Alkylamino- and 7-alkoxyaminopyrido[3,2-d]pyrimidines were also irreversible inhibitors with equal or superior potency against the isolated enzyme but were less effective in the cellular autophosphorylation assays. Both quinazoline- and pyrido[3,2-d]pyrimidine-6-acrylamides bound at the ATP site alkylating cysteine 773, as shown by electrospray ionization mass spectrometry, and had similar rates of absorptive and secretory transport in Caco-2 cells. A comparison of two 7-propoxymorpholide analogs showed that the pyrido[3,2-d]pyrimidine-6-acrylamide had greater amide instability and higher acrylamide reactivity, being converted to glutathione adducts in cells more rapidly than the corresponding quinazoline. This difference may contribute to the obsd. lower cellular potency of the pyrido[3,2-d]pyrimidine-6-acrylamides. Selected compds. showed high in vivo activity against A431 xenografts on oral dosing, with the quinazolines being superior to the pyrido[3,2-d]pyrimidines. Overall, the quinazolines proved superior to previous analogs in terms of aq. soly., potency, and in vivo antitumor activity, and one example (CI 1033) has been selected for clin. evaluation.

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 1998:323483 CAPLUS
DN 129:119500
TI Inhibitors of the epidermal growth factor receptor protein tyrosine kinase. A quantitative structure-activity relationship analysis

AU Singh, P.; Kumar, R.
CS Department Chemistry, S. K. Government College, Sikar, 332001, India
SO Journal of Enzyme Inhibition (1998), 13(2), 125-134
CODEN: ENINEG; ISSN: 8755-5093
PB Harwood Academic Publishers
DT Journal
LA English
IT **171745-06-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(quant. structure-activity relationship of inhibitors of the epidermal growth factor receptor protein tyrosine kinase)
RN 171745-06-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



AB Hansch and Free-Wilson analyses are described on a data set, 4-anilinoquinazolines [the analogs of 4-(3-bromo-anilino)-6,7-dimethoxy quinazoline: PD 153035], as inhibitors of the epidermal growth factor receptor protein tyrosine kinase. These analyses have helped to ascertain the role of different substituents in explaining the obsd. inhibitory activities. From both approaches, it is concluded that the combined electron-donating nature of R1- and R2-substitutions of the quinazoline ring and the electron-withdrawing nature of the X-substitution of the anilino-ring are beneficial for increasing the inhibition activity of a compd. Further, the sym. alkoxy substituents present at the R1- and R2-positions are also engaged in a steric interaction which was detd. quant. through the parabolic relationship between the activity and combined molar refraction parameter, .SIGMA.MR of the substituents.

L4 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 1997:696745 CAPLUS
DN 128:3695
TI Preparation of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors
IN Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong; et al.
PA Warner-Lambert Company, USA; Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong
SO PCT Int. Appl., 193 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9738983	A1	19971023	WO 1997-US5778	19970408
	W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
				US 1996-15351P P	19960412
	CA 2249446	AA	19971023	CA 1997-2249446	19970408
				US 1996-15351P P	19960412
	AU 9724463	A1	19971107	AU 1997-24463	19970408
	AU 725533	B2	20001012		
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
	EP 892789	A1	19990127	EP 1997-920213	19970408
	EP 892789	B1	20020227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
	CN 1218456	A	19990602	CN 1997-194458	19970408
				US 1996-15351P P	19960412
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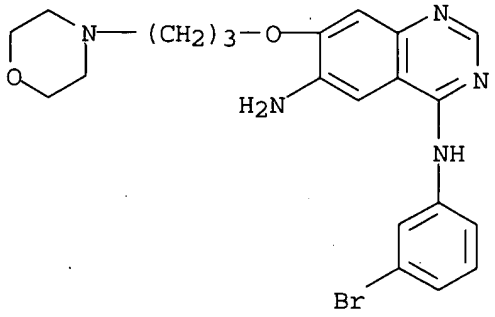
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
	JP 2000508657	T2	20000711	JP 1997-537173	19970408
	JP 3370340	B2	20030127		
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
	AT 213730	E	20020315	AT 1997-920213	19970408
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
	ES 2174250	T3	20021101	ES 1997-920213	19970408
				US 1996-15351P P	19960412
	ZA 9703060	A	19971104	ZA 1997-3060	19970410
				US 1996-15351P P	19960412
	BG 63160	B1	20010531	BG 1998-102811	19981001
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
	NO 9804718	A	19981209	NO 1998-4718	19981009
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408
	KR 2000005364	A	20000125	KR 1998-708086	19981010
				US 1996-15351P P	19960412
	US 6344459	B1	20020205	US 1999-155501	19990608
				US 1996-15351P P	19960412
				WO 1997-US5778 W	19970408

OS MARPAT 128:3695
IT **198961-78-3P 198961-80-7P 198961-82-9P**
198961-84-1P 198961-86-3P 198961-87-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-quinazolinylacrylamides and analogs as tyrosine kinase

inhibitors)

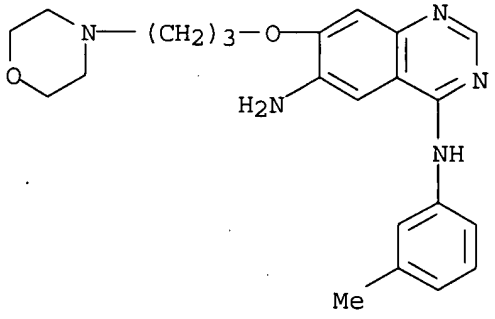
RN 198961-78-3 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



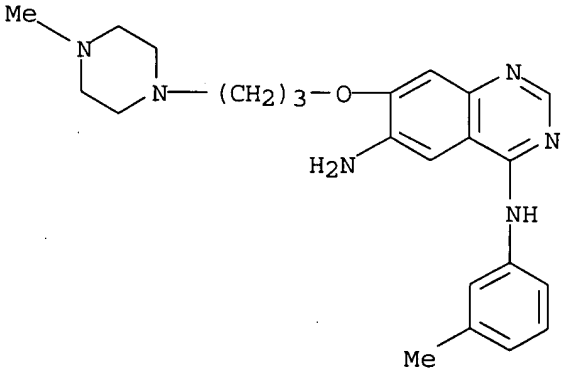
RN 198961-80-7 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-morpholinyl)propoxy]- (9CI) (CA INDEX NAME)



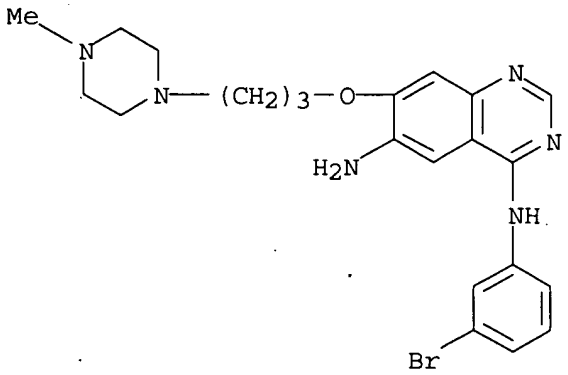
RN 198961-82-9 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-methylphenyl)-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)

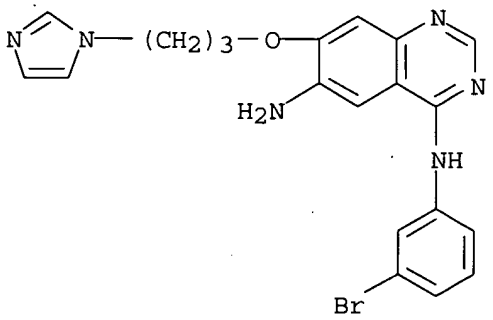


RN 198961-84-1 CAPLUS

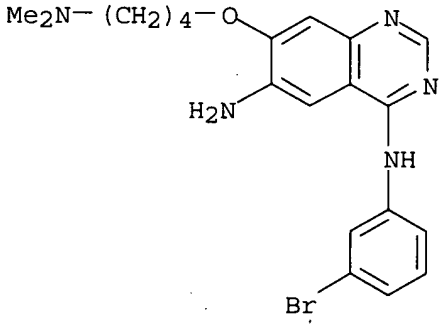
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(4-methyl-1-piperazinyl)propoxy]- (9CI) (CA INDEX NAME)



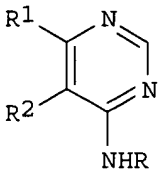
RN 198961-86-3 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[3-(1H-imidazol-1-yl)propoxy]- (9CI) (CA INDEX NAME)



RN 198961-87-4 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-[4-(dimethylamino)butoxy]- (9CI) (CA INDEX NAME)



GI



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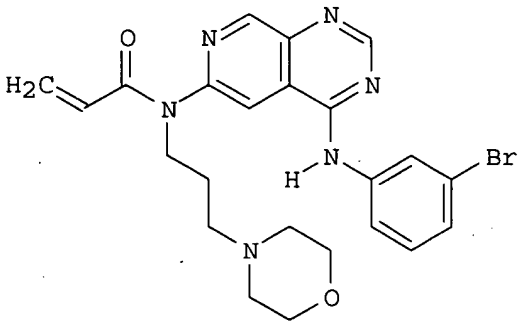


II

AB Title compds. [I; R = (CHR6)pR9; R1R2 = CH:CR7CR8:CH, CH:CR7CR8:N, CH:CR7N:CH, etc.; R6 = H or alkyl; 1 of R7,R8 = Z1Z2R10 and the other = OR4, SR4, NHR3; R3,R4 = (un)substituted alkyl, heterocyclylalkyl, etc.; R9 = (un)substituted Ph; R10 = CR11:CHR5, C.tplbond.CR5, CR11:C:CHR5; R5 = H, halo, alkyl, Ph, etc.; R11 = H, halo, alkyl; Z1 = bond, O, (alkyl)imino, CH2, etc.; Z2 = CO, SO, P(O)(OH), etc.; p = 0 or 1] were prepd. Thus, I (R = C6H4Br-3, R1R2 = CH:NCR8:CH, R8 = F) was condensed with 3-morpholinoprpanamine and the product acylated by CH2:CHCOCl to give title compd. II. Data for biol. activity of I were given.

L4 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 1996:756470 CAPLUS
DN 126:18889
TI Preparation of 6-(2-methoxyethylamino)-7-methoxy-4-(3'-methylanilino)quinazoline cell proliferation inhibitor
IN Barker, Andrew John
PA Zeneca Limited, UK
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9633981	A1	19961031	WO 1996-GB962	19960423
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
				GB 1995-8535 A	19950427
	AU 9653434	A1	19961118	AU 1996-53434	19960423
				GB 1995-8535 A	19950427
				WO 1996-GB962 W	19960423
	EP 823901	A1	19980218	EP 1996-910135	19960423
	EP 823901	B1	20001018		
	R: CH, DE, FR, GB, IT, LI				
				GB 1995-8535 A	19950427
				WO 1996-GB962 W	19960423
	JP 11504034	T2	19990406	JP 1996-532253	19960423

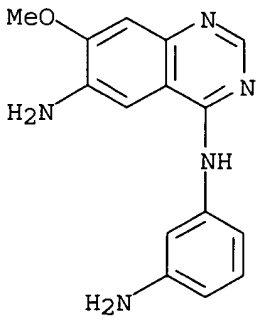
				GB 1995-8535	A 19950427
				WO 1996-GB962	W 19960423
	US 5952333	A	19990914	US 1997-930044	19970926
				GB 1995-8535	A 19950427
				WO 1996-GB962	W 19960423

OS MARPAT 126:18889

IT **184473-34-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 6-(2-methoxyethylamino)-7-methoxy-4-(3'-methylanilino)quinazoline cell proliferation inhibitor)

RN 184473-34-5 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-aminophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



AB 6-(2-Methoxyethylamino)-7-methoxy-4-(3'-methylanilino)quinazoline, useful as a cell-inhibiting tyrosine kinase receptor inhibitor for the treatment of proliferative diseases such as cancer (no data), prepd. by the reaction of 2-methoxyacetaldehyde di-Me acetal and 6-amino-7-methoxy-4-(3'methylanilino)quinazoline in the presence of NaBH4, demonstrated a IC50 of 0.01 .mu.M against the enzyme EGF receptor tyrosine kinase.

L4 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2003 ACS

AN 1996:483485 CAPLUS

DN 125:142741

TI Prepn. of N-phenyl-4-quinazolinamines for the treatment of proliferative diseases

IN Brown, Dearg Sutherland; Morris, Jeffrey James; Thomas, Andrew Peter

PA Zeneca Limited, UK

SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9615118	A1	19960523	WO 1995-GB2606	19951108

W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

			GB 1994-22866	19941112
			GB 1995-7308	19950407
CA 2200871	AA	19960523	CA 1995-2200871	19951108
			GB 1994-22866	19941112
			GB 1995-7308	19950407
AU 9538130	A1	19960606	AU 1995-38130	19951108
AU 703328	B2	19990325		
			GB 1994-22866	19941112
			GB 1995-7308	19950407
			WO 1995-GB2606	19951108
EP 790986	A1	19970827	EP 1995-936044	19951108
EP 790986	B1	19990120		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
			GB 1994-22866	19941112
			GB 1995-7308	19950407
			WO 1995-GB2606	19951108
JP 10508616	T2	19980825	JP 1995-515816	19951108
			GB 1994-22866	19941112
			GB 1995-7308	19950407
			WO 1995-GB2606	19951108
AT 175962	E	19990215	AT 1995-936044	19951108
			GB 1994-22866	19941112
			GB 1995-7308	19950407
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ZA 9509572	A	19960513	ZA 1995-9572	19951110
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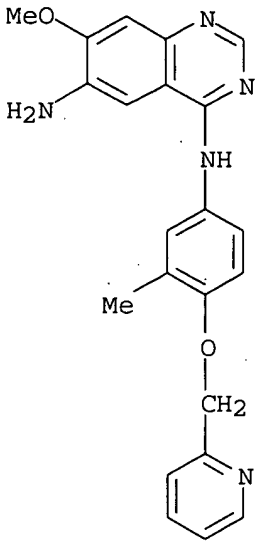
FI 9701970	A	19970507	FI 1997-1970	19970507
			GB 1994-22866	19941112
			GB 1995-7308	19950407
			WO 1995-GB2606	19951108
NO 9702152	A	19970512	NO 1997-2152	19970509
			GB 1994-22866	19941112
			GB 1995-7308	19950407
			WO 1995-GB2606	19951108
US 5821246	A	19981013	US 1997-836362	19970521
			GB 1994-22866	19941112
			GB 1995-7308	19950407
			WO 1995-GB2606	19951108

OS MARPAT 125:142741

IT **179688-72-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N-phenylquinazolinamines as tyrosine kinase inhibitors)

RN 179688-72-3 CAPLUS

CN 4,6-Quinazolinediamine, 7-methoxy-N4-[3-methyl-4-(2-pyridinylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



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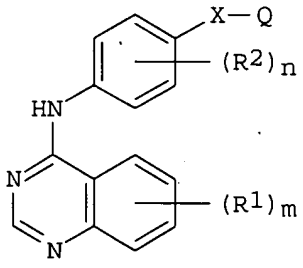

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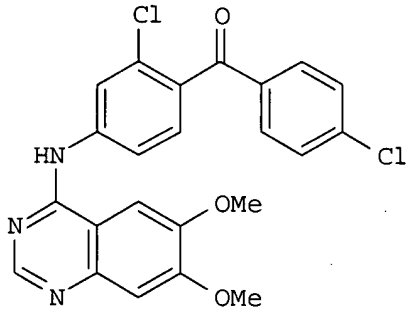

II

AB The title compds. I (m = 1-3; R1 = halo, hydroxy, amino, ureido, etc.; n = 0-3; R2 = halo, trifluoromethyl, hydroxy, amino, nitri, cyano, alkyl; X = carbonyl, methine, O,S, etc.) were disclosed. I were claimed for the use as receptor tyrosine kinase inhibitors and for treatment of proliferative disease such as cancer. An example compd. is the chlorophenyl [(quinazolinyl)amino]phenyl methanone II.

L4 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 1996:476843 CAPLUS
DN 125:142761
TI Quinazoline derivatives
IN Barker, Andrew John
PA Zeneca Limited, UK
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9616960	A1	19960606	WO 1995-GB2768	19951128
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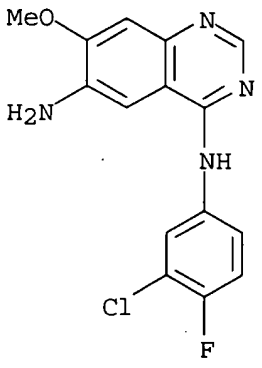
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
				GB 1994-24233	19941130
	AU 9539330	A1	19960619	AU 1995-39330	19951128
				GB 1994-24233	19941130
				WO 1995-GB2768	19951128
	EP 794953	A1	19970917	EP 1995-937126	19951128
	EP 794953	B1	19990506		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
				GB 1994-24233	19941130
				WO 1995-GB2768	19951128
	JP 10509972	T2	19980929	JP 1995-518417	19951128
				GB 1994-24233	19941130
				WO 1995-GB2768	19951128
	AT 179708	E	19990515	AT 1995-937126	19951128
				GB 1994-24233	19941130
	US 5955464	A	19990921	US 1997-860088	19970522
				GB 1994-24233	19941130
				WO 1995-GB2768	19951128

OS MARPAT 125:142761

IT **179552-75-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of tyrosine kinase inhibiting imidazolylquinazolines)

RN 179552-75-1 CAPLUS

CN 4,6-Quinazolinediamine, N4-(3-chloro-4-fluorophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



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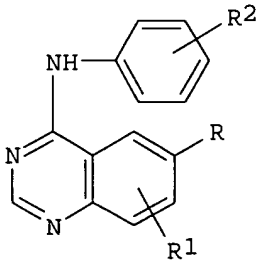
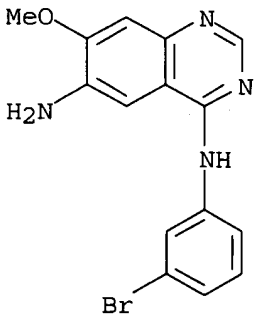


I

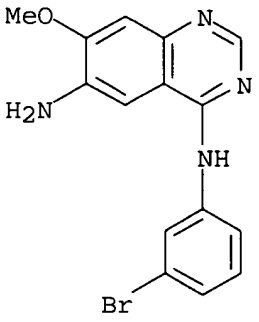
AB The invention concerns quinazoline derivs. I (m = 1, 2; R1 = H, halo, alkyl, alkoxy; n = 1-3; R2 = H, OH, halo, alkyl; R = 5- or 9-membered nitrogen-linked heteroaryl moiety contg. up to four nitrogen heteroatoms, or R = a 5-, 6-, 9- or 10-membered nitrogen-linked unsatd. heterocyclic moiety contg. up to three nitrogen heteroatoms which bears one or two substituents selected from oxo and thioxo) and the use of the receptor tyrosine kinase inhibitory properties of the compds. in the treatment of proliferative diseases such as cancer. Among the approx. 15 title compds. prepd., 4-(3-methylanilino)-, 4-(3-chloro-4-fluoroanilino)-, 4-(4-benzoyl-3-chloroanilino)-, and 4-[3-methyl-4-(2-pyridylmethoxy)anilino]-6-(1-imidazolyl)quinazolines were claimed.

L4 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 1996:312235 CAPLUS
DN 125:25623
TI Structure-activity relationships for 4-anilinoquinazolines as potent inhibitors at the ATP binding site of the epidermal growth factor receptor in vitro
AU Denny, William A.; Rewcastle, Gordon W.; Bridges, Alexander J.; Fry, David W.; Kraker, Alan J.
CS Cancer Research Lab., Univ. Auckland School Medicine, Auckland, 92019, N. Z.
SO Clinical and Experimental Pharmacology and Physiology (1996), 23(5), 424-427
CODEN: CEXPB9; ISSN: 0305-1870
PB Blackwell
DT Journal
LA English
IT **171745-06-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anilinoquinazolines as potent inhibitors at ATP binding site of epidermal growth factor receptor)
RN 171745-06-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



AB Structure-activity relationships are described for the inhibition of the tyrosine kinase activity (phosphorylation of a fragment of phospholipase Cg1) of the epidermal growth factor receptor (EGFR) by 4-anilinoquinazolines. These compds. are competitive inhibitors at the ATP binding site. The preferred side chain is anilino-, substituted at the 3-position with small lipophilic groups. The quinazoline moiety is absolutely required for activity, but substituents on the quinazoline greatly modulate potency, with electron-donating groups favored. The most potent analog, the 6,7-dimethoxy deriv., has an IC50 of 29 pmol/L and a very high selectivity for the EGFR over other tyrosine kinase enzymes. The present study shows that it is possible to identify small mols. that are very potent, yet highly selective, inhibitors of a single component of the growth signal transduction pathway in cells.

L4 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 1995:983167 CAPLUS
DN 124:21051
TI Tyrosine kinase inhibitors: unusually steep structure-activity relationship for analogs of 4-(3-bromoanilino)-6,7-dimethoxyquinazoline (PD 153035), a potent inhibitor of the epidermal growth factor receptor
AU Bridges, Alexander J.; Zhou, Hairong; Cody, Donna R.; Rewcastle, Gordon W.; McMichael, Amy; Showalter, H. D. Hollis; Fry, David W.; Kraker, Alan J.; Denny, William A.
CS Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48106-1047, USA
SO Journal of Medicinal Chemistry (1996), 39(1), 267-76
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
IT **171745-06-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epidermal growth factor receptor tyrosine kinase inhibitors: structure-activity relations for analogs of (bromoanilino)dimethoxyquinazoline (PD 153035))
RN 171745-06-5 CAPLUS
CN 4,6-Quinazolinediamine, N4-(3-bromophenyl)-7-methoxy- (9CI) (CA INDEX NAME)



AB 4-(3-Bromoanilino)-6,7-dimethoxyquinazoline (PD 153035) is a very potent inhibitor (IC50 0.025 nM) of the tyrosine kinase activity of the EGF receptor, binding competitively at the ATP site. Structure-activity relations for close analogs of PD 153035 are very steep. Some derivs. have IC50 .ltoreq.80-fold better than predicted from simple additive binding energies, yet analogs possessing combinations of similar Ph and quinazoline substituents do not show this supra-additive effect. Some substituents which are mildly deactivating by themselves can be strongly activating when used in the correct combinations; therefore, certain substituted analogs may induce a change in conformation of the receptor when they bind. There is some bulk tolerance for substitution in the 6- and 7-positions of the quinazoline, so that PD 153035 is not the optimal inhibitor for the induced conformation. 4-(3-Bromoanilino)-6,7-diethoxyquinazoline shows an IC50 of 0.006 nM, making it the most potent inhibitor of the tyrosine kinase activity of the EGF receptor yet reported.

L4 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2003 ACS
AN 1994:217715 CAPLUS
DN 120:217715
TI Quinazoline tyrosine kinase-inhibiting anticancer agents
IN Barker, Andrew J.
PA Zeneca Ltd., UK
SO Can. Pat. Appl., 99 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

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US 5457105	A	19951010	US 1994-284293	19940802
				GB 1992-1095 A 19920120
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				US 1993-5280 B119930119
US 5616582	A	19970401	US 1995-490666	19950615
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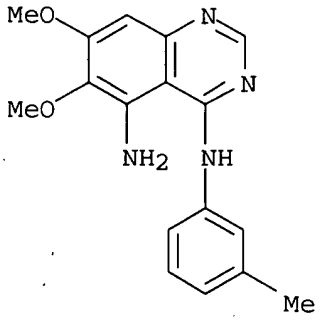
OS MARPAT 120:217715

IT **153437-12-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of, as intermediate in prepn. of quinazoline tyrosine .kinase-inhibiting anticancer agents)

RN 153437-12-8 CAPLUS

CN 4,5-Quinazolinediamine, 6,7-dimethoxy-N4-(3-methylphenyl)- (9CI) (CA

INDEX NAME)



IT **153437-18-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of, as tyrosine kinase-inhibiting anticancer agent)
RN 153437-18-4 CAPLUS
CN 4,6-Quinazolinediamine, 7-methoxy-N4-(3-methylphenyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

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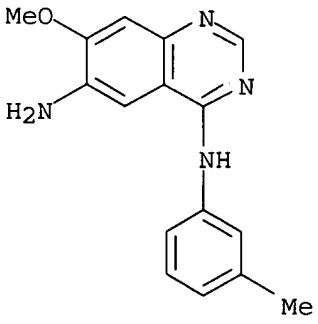

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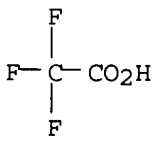
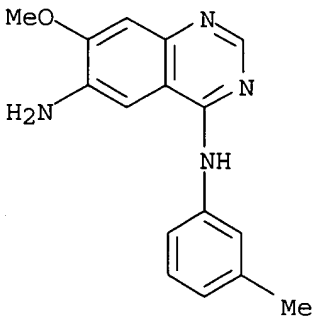


IT **153437-17-3P**

RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(tyrosine kinase-inhibiting anticancer agent)
RN 153437-17-3 CAPLUS
CN 4,6-Quinazolinediamine, 7-methoxy-N4-(3-methylphenyl)- (9CI) (CA INDEX NAME)



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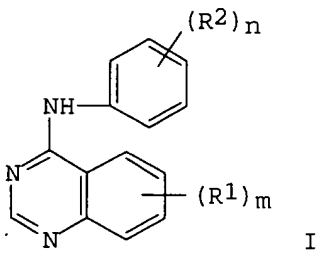

I

AB The title compds. I [R1 = HO, (un)substituted amino, carboxy, carbamoyl, ureido, etc.; R2 = H, HO, halogen, CF3, NH2, NO2, CN, (un)substituted C1-4 alkyl, etc.; m = 1-3; n = 1, 2], useful as tyrosine kinase-inhibiting anticancer agents (no data), are prepd. and I-contg. formulations presented. Thus, 4-chloro-6,7-dimethoxyquinazoline was condensed with 3-MeC6H4NH2, producing 6,7-dimethoxy-4-(3'-methylanilino)quinazoline hydrochloride, m.p. 248-249.degree..

=> s l4 and Tyrosine kinase
L5 18 L4 AND TYROSINE KINASE

=> d his

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L2 7 S L1
L3 82 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 14:39:27 ON 01 JUL 2003
L4 24 S L3

L5 18 S L4 AND TYROSINE KINASE

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	137.71	286.07

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-15.62	-15.62

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